Archives of Neurology and Psychiatry

VOLUME 51 FEBRUARY 1944 NUMBER 2

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STUDIES IN REFLEXES

HISTORY, PHYSIOLOGY, SYNTHESIS AND NOMENCLATURE: STUDY I

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The subject of this clinical and literary study is a discussion of some of the diagnostically most important reflexes from a practical neurologic standpoint. It deals with their history, physiology, technic of elicitation, synthesis and nomenclature, with emphasis on the synthesis of the existing reflexes and the simplification of their nomenclature.

In 1927, a leading Polish neurologist,[1] in an abstract of a Russian article on reflexes, said:

> In any event, in view of the wealth of reflexes to be elicited from the soles of the feet, which in summer are usually dirty, the practitioner should be extremely grateful to the neurologist who would contribute something concrete to the unification and understanding of the physiogenesis of these reflexes; he would thus spare the clinician the necessity of examination for most of them.

On the same page, a German neurologist,[2] in discussing a Polish study on reflexes stated:

> . . . It is gratifying that now, from several angles, the rediscovery of reflexes is undergoing critical scrutiny. . . . Indeed, there would soon be more reflexes, especially of the lower extremities, than there are muscles and bones. A systematic synthesis would be appropriate.

An attempt at such a synthesis is made here. Dorland [3] lists nearly two hundred and fifty reflexes, and a few more are given under the heading of "Signs." Seventy-six new pathologic reflexes were described in the period from 1918 to 1943, according to the statistics of Fröhlich.[4] No wonder then that the reader of neurologic textbooks, journals and hospital charts is confused and puzzled by the descriptions of reflexes he finds there. He meets a great number of unfamiliar eponyms, which often are not contained in any medical dictionary or textbook. Various authors attribute the discovery of the same reflex to different persons and name it accordingly. A single reflex may be named according to the site of its elicitation, the muscles involved, the ensuing movement, the joint on which it acts or the nerves involved. Some reflexes are called signs or phenomena; some are designated by a proper name only, occasionally with an attached numeral. Thus one may read: "Bechterew 2 is negative," or "Bing 1 and 2 are strongly positive." To the authors of these names, that which is conveyed by them is self explanatory—not so to the reader. A leading European neurologist, in reporting a case in 1937, used in a single paragraph, and without further comment, fourteen proper names (including his own) to describe the reflexes in his case. Many an author, in his enthusiasm over the discovery of what he thinks is a new reflex, does not correlate his reflex with the phenomena already recognized. It is thus not clear whether the "new" reflex is a new phenomenon at all or whether it represents merely a new technic by which an old and familiar reflex is brought to light. Thus it happens that the old reflexes have been rediscovered several times, and many a "recently discovered" reflex is actually only a modification of an old one or a combination of multiple reflexes.

Many a reflex has been "discovered" by one author after another, often at intervals of several decades. These authors, anxious to attach their own names to a "new" reflex, have neglected completely the work of their predecessors. The

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Dedicated, in deep gratitude, to Dr. Langley Porter, dean of the University of California Medical School, 1927 to 1941.

Read in part at the Sixty-Seventh Annual Meeting of the American Neurological Association, Chicago, June 5, 1942.

1. Markov, D.: Receptorenzonen für Reflexe vom Typus Mendel-Bechterew-Rossolimo-Žukovskij-Kornilov, Sovrem. psichonevrol. **3**:64, 1926; abstracted by Higier, H.: Zentralbl. f. d. ges. Neurol. u. Psychiat. **45**:726, 1927.

2. Sagin, K.: Der Reflex des "Malleolus externus" und das Piotrowskische Phänomen, Monatschr. f. Psychiat. u. Neurol. **61**:188, 1926; abstracted by Loewy-Hattendorf, E.: Zentralbl. f. d. ges. Neurol. u. Psychiat. **45**:726, 1927.

3. Dorland, W. A. N.: The American Illustrated Medical Dictionary, ed. 19, Philadelphia, W. B. Saunders Company, 1941, p. 1230.

4. Fröhlich, J.: Die Bereicherung unserer Kenntnisse über pathologische Reflexe in den letzten 15 Jahren, Inaug. Dissert., Basel, 1935.

history of reflexes provides an interesting chapter in the book of human vanity—a chapter often not lacking in tragicomic elements.

Many a phenomenon which is not at all reflexive in its character is designated as a reflex. In a recently published book, for instance, the leg sign of Barré is wrongly called a reflex. With this valuable sign of hemiplegia, the patient, while lying prone on his stomach with his legs flexed to a vertical position at the knee, is unable to maintain this position on the side of the pyramidal lesion and gradually extends the affected leg. This phenomenon is of course not a reflex but simply a motor response to the inequality in strength of the extensor and flexor muscles of the legs in hemiplegia. In a recently published textbook, the diminution of the palpable vibrations of the orbicularis oculi muscle associated with facial palsy of long standing has been designated as a reflex. This phenomenon is by no means a reflex but is simply an expression of decreased innervation. In a reference book published in 1939, the platysma sign of Babinski is called a reflex, whereas it simply indicates the weakness of the platysma muscle on the side of hemiplegia.

Much further confusion has been caused by the fact that true deep muscle reflexes are not always distinguished from reflex phenomena which belong in quite a different category, i. e., associated movements, reflexes of spinal automatism, defense reflexes and postural reflexes. The "new tendon stretch reflex," recently described by Gonda,[5] is in fact a modification of the Marie-Foix maneuver for elicitation of the flexor withdrawal reflex. This is a postural, a coordinated, reflex, and not a muscle stretch reflex (Wartenberg[6]). Furthermore, the distinction between the so-called deep and the superficial reflexes is not always made clear.

Much has been done in standardization of the nomenclature of disease, but little in standardization of the terms used to designate signs and symptoms and less in description of the numerous reflexes. At present there is no need for more reflexes or for more variations in the technic of their elicitation. The last decades brought a real "inflation" in this respect. What is actually needed is a simplification, a synthesis and correlation of the many reflexes already in existence. The mere listing of the reflexes, together with their various proper names, as practiced in many a textbook, imposes a great burden on the student and does not in any sense present an appropriate physiologic approach to the problem.

For the preparation of this paper, which attempts a systematic synthesis of some of the numerous deep reflexes, the literature, especially the earliest, which appeared in six languages, including the Russian, was studied in the original. This review of the literature, though extensive, is of course by no means exhaustive. Such a survey would have required volumes. Moreover, war conditions necessitated a sharp curtailment in the original plan for a monographic presentation of the subject.

BASIC PRINCIPLES

For a basic understanding of the problem, I shall first outline in brief form a few general tenets applicable to all reflexes under discussion.

1. It is permissible from a physiologic standpoint to assume that every striated muscle, as it contracts on direct mechanical, electrical or voluntary stimulation, contracts also on reflexive stimulation. The most important reflexive stimulus of the muscle consists of a sudden, brief concussion and stretching of the muscle tissue. Here the most essential stimulus—perhaps the only one—is a sudden, quick pull, exerted longitudinally. The emphasis lies on the sharpness and brevity of the stroke. A slow stroke, even though its range is greater, is ineffective. The muscle reacts to this sudden stretching with contraction, which constitutes what is called the deep, or tendon, reflex. In general, when one speaks of a deep reflex as a muscle stretch reflex, one has in mind a sudden, brisk stretching, a jarring of the muscle, so to speak, and not a slow stretching, which leads to a change in position. Many other reflex phenomena, such as associated movements, postural reflexes and support reactions, are elicited through change in position, that is, in a practical sense, through stretching of some muscles. But such responses are not in any sense the muscle stretch reflexes which are discussed here. Foerster wrongly criticized Hoffmann's concept of the reflexes since he did not differentiate clearly between these two types of muscle stretch phenomena. Nearly all striated muscles can be reflexively stimulated by quick stretching. Lastly, such a reflex has been demonstrated in the diaphragm (Trömner[7]). Only from the ocular muscles, thus far, have such reflexes not been obtained.

2. These muscle stretch reflexes serve, and did serve still more earlier in phylogenetic development, as a useful protective mechanism,

5. Gonda, V.: A New Tendon Stretch Reflex, Arch. Neurol. & Psychiat. **48**:531 (Oct.) 1942.

6. Wartenberg, R., in discussion on Gonda, V.: A New Tendon Stretch Reflex and Its Significance in Lesions of the Pyramidal Tracts, Tr. Am. Neurol. A. **68**:111, 1942.

7. Trömner, E.: Ein (neuer) Zwerchfellreflex, Deutsche Ztschr. f. Nervenh. **102**:157, 1928.

especially in standing and walking. They have the task of fixing the position of the joints and of counteracting quickly the influence of every sudden external agent that changes the position of the joint. Some muscles react with contraction more easily and strongly to stretching than others, the threshold of response depending on their function. Muscles which are physiologically stronger than their antagonists, as well as muscles which show a greater tendency to contraction in spastic paralysis, respond more easily to passive stretching. The extensor muscles of the legs (the quadriceps muscle and the muscles of the calf) show better developed deep reflexes than the flexor muscles. Undoubtedly this difference has to do with their function in the maintenance of correct posture in standing and walking. Normal, rapid function of the quadriceps reflex will prevent, compensate for and ease any sudden, momentary collapse of the body and is essential for correct posture. A quick reflexive contraction of the muscles of the calf on being stretched will prevent the body from falling forward; contraction of the flexors of the toes will help the foot to clinch the ground when the body's balance is endangered. In the arms, the reflexes of the pronators are more excitable than those of the supinators. Some muscles are so situated that they are mechanically more accessible to passive stretching than others.

3. The strength of the reflex action of the various muscles of any person thus differs widely. This strength also varies greatly from one person to another. Some normal persons show deep muscle reflexes only in traces, even with the most delicate technic. The contraction of a muscle on being stretched may exist in latent form and become distinct, or apparent at all, only when there is a functional or an organic increase in muscle tonus. Thus, a pyramidal lesion may (*a*) increase the existing reflexes and (*b*) bring the reflexes which are latent to the fore. Here the presence of these reflexes does not of itself mean the presence of a pyramidal lesion, though the reflexes are especially likely to appear if such a lesion exists. It is essential, therefore, to keep in mind the fact that the appearance of some reflexes—usually latent—in the presence of a pyramidal lesion does not mean that the reflexes are new, but rather that they represent the pathologic exaggeration of normal reflexes which exist in latent form. Thus, if a reflex, usually latent, is clearly seen, it may indicate a pyramidal lesion, but not necessarily so. From the standpoint of diagnosis, this point should be stressed.

4. Since concussion of the muscle and its stretching constitute the true cause of the deep muscle reflex, the point from which this response may be achieved is not essential. It is irrelevant whether the concussion comes from the tendon, from the neighboring joints or from bone, or is obtained through a broad mass percussion of the muscle itself. No point has any monopoly; every muscle can be stretched, and its reflex contraction is effected from many points. In cases of hyperreflexia even a slight concussion—direct or indirect—of the bone to which the muscle is attached is sufficient to provoke its reflexive contraction.

5. Every muscle crosses one or more joints and is therefore comparable to a tautly drawn bowstring. Sudden stretching of such a string may be achieved by a force acting either on the plane or on the convex side of this bow mechanism. The tapping of the muscle itself, of its point of origin or of its point of insertion corresponds to the tapping of the taut string at any of its points. But one is able to effect a stretching of the string also by tapping the convex side of the bow mechanism, especially at its top. One depresses the top of the arch and thus causes a sudden stretching of the bowstring, representing the muscles. This possibility of elicitation of a deep muscle reflex, not by attack on the muscle itself but by stimulation on the convex side of the arch—the bone—deserves to be stressed, since it offers much to the comprehension of many misunderstood and misnamed reflex phenomena.

6. The concussion and stretching of a muscle that leads to its reflex contraction can be achieved not only from points located directly on either side of the "arch" but from neighboring, and even distant, points. Here the bone acts as transmitter of the mechanical insult. It is possible to elicit the reflexes from remote places, particularly in cases in which there is functional or organic reflex hyperirritability. The older neurologists, in referring to such cases, spoke of "an extension of the reflexogenous zones"—an incorrect and misleading term.

7. The transmission of concussion through the bone makes it understandable that under favorable conditions a single tap with the reflex hammer may affect several functionally different muscles and thus evoke multiple, but completely independent, unrelated reflexes. One is apt to overlook this possibility in eliciting a particular reflex, since the attention is concentrated on the action of the corresponding muscle. Practically, however, one often elicits more than one reflex more or less distinctly, the complexity of the response depending on the position of the limb, the strength and direction of the stroke, the relative strength of the reflexes and the

degree of general reflex irritability. Moreover, one might even say it is difficult to avoid elicitation of multiple reflexes with a single tap and to obtain the desired effect on a single muscle.

8. Since each of the clinically important reflexes can be elicited, even in normal persons, in three, four, or even more, ways, a boundless confusion would result if every such possible reflex elicited were dubbed a special reflex and given a specific, or even a proper, name. The tendency should be to name the reflex according to the acting muscles, not the point of stimulation. For a given reflex the muscle is always the same, but the place of stimulation may vary considerably. It is clinically essential to know whether the reflex is present, altered or absent, but it is not necessary to know from which point this can be demonstrated. If, in describing the reflexes, one wishes to be exact, one may note the special technic of their elicitation without resorting to new or proper names.

If, in interpreting and naming the reflexes, one shifts the focus of attention from the point of elicitation to the muscle whose action is provoked, an essential simplification, a better physiologic understanding and a distinct didactic advantage result. Then the existing reflex phenomena may be easily assigned to their proper places, future discoveries in this field may be readily appraised and classified and the uncritical discovery of "new" reflexes may be checked. While the abolition of proper names in the nomenclature of reflexes is generally favored, it is still well to apply them temporarily to really new reflexes or in exceptional or classic phenomena. The Babinski toe sign may represent such a reflex.

9. What has been said thus far refers to the so-called deep reflexes, which are often designated as tendon, bone, periosteal, osteoperiosteal, osteotendon, joint, fascial or aponeurotic reflexes. Since the investigations of Sternberg,[8] in 1893, and of Hoffmann,[9] in 1922, it has been known that the receptors of the "tendon and periosteal" reflexes lie not in the tendon or in the periosteum but in the muscle itself. Yet, in a recent article, Guillain[10] said: "The tendon and periosteal reflexes are abolished." In the most recent Spanish textbook of neurology, Barraquer Ferré, de Gispert Cruz and Castañer Vendrell[11] distinguished between tendon reflexes and osteoperiosteal reflexes. In another Spanish textbook, published in 1939, Litter and Wexselblatt[12] spoke of tendon and periosteal reflexes. Even Kinnier Wilson, in his fundamental work on neurology, spoke of bone and tendon reflexes. It is extremely difficult, to be sure, to find an appropriate adjective in which is condensed the meaning of such a complex phenomenon as a reflex. But these terms, though widely used, are objectionable since they are not in accordance with the modern, physiologically based concept of the nature of these reflexes. The time-honored term "tendon reflexes," introduced by Erb in 1875, is especially misleading and should not be used at all. From a neurophysiologic standpoint the tendon, so to speak, is passive, dead tissue, and no stimulation of the tendon can evoke any reflex action unless the muscle tissue is influenced through the tendon. There is no such thing as a "tendon stretch reflex." One can elicit the deep reflexes without touching the tendon—for instance by tapping the patella downward to obtain the quadriceps muscle reflex. Furthermore, reflexes can be obtained in muscles having no tendons, such as the masseter muscle. Long ago Gowers[13] emphasized that the intervention of tendons is not necessary for the production of "tendon reflexes." The importance of the tendon lies only in the fact that, like a bridle, it controls the whole muscle by presenting a tough, small bundle, which takes little space and is easily accessible to the stroke of the reflex hammer. Thus the muscle tendon serves only as a transmitter of the stretch stimulus from the point of application to the muscle fibers. Gowers pointed out that the one condition which all "tendon reflexes" have in common is the passive tension which is essential for their occurrence, and he also suggested that they be termed myotatic contractions —from the Greek word τεινειν, meaning to "extend." Earlier in 1880, Gowers[14] stated that the term "tendon reflex" is inaccurate and misleading. He asserted that the achilles reflex is essentially a muscle reflex phenomenon and not a tendon reflex.

It is hardly necessary to elaborate on the fact that the reflexes in question are not periosteal,

8. Sternberg, M.: Die Sehnenreflexe und ihre Bedeutung für die Pathologie der Nervensystems, Leipzig, F. Deuticke, 1893.

9. Hoffmann, P.: Untersuchungen über die Eigenreflexe menschlicher Muskeln, Berlin, Julius Springer, 1922.

10. Guillain, G.: Radiculoneuritis with Acellular Hyperalbuminosis of Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **36**:975 (Nov.) 1936.

11. Barraquer Ferré, L.; de Gispert Cruz, I., and Castañer Vendrell, E.: Tratado de enfermedades nerviosas, Barcelona, Salvat Editores, S. A., 1936-1940.

12. Litter, M., and Wexselblatt, M.: Tratado de neurologia, Buenos Aires, El Ateneo, 1939.

13. Gowers, W. R.: A Manual of Diseases of the Nervous System, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1907, vol. 1, p. 26.

14. Gowers, W. R.: Diagnosis of Diseases of the Spinal Cord, London, J. & A. Churchill, 1880, p. 25.

either in origin or in mode of elicitation. The deep reflex cannot be abolished even if the sensibility of the periosteum has been completely eliminated by procaine. The so-called radioperiosteal reflex is not periosteal at all. It is a stretch reflex of the brachioradialis muscle. The periosteum is only the point of application of the stretch stimulus. There are likewise among the deep reflexes no fascial, bone or joint reflexes. The sensibility of the joints, for instance, does not play any role. These structures serve only to transmit the stretch stimulus. The deep reflexes are physiologically muscle stretch reflexes and should be so called. But the custom and brevity make it desirable to retain the old term "deep reflexes."

10. Reflexes which do not fit into the regular reflex pattern are often called "paradoxic," "inverted" or "antagonistic." These terms should not be used. There is nothing paradoxic, inverted or antagonistic about them. It will be shown in the discussion of individual reflexes that these phenomena are simply occasional forms of well known deep reflexes appearing under certain conditions and depending on particular technics applied in their elicitation. They are easily understandable, normal phenomena.

11. The second large group of reflexes are called superficial, or "skin," reflexes, in contrast to the deep reflexes. Hoffmann called them *Fremdreflexe,* since the stimulus initiating the contraction is applied not to the muscle itself but outside the muscle. In the superficial reflex a stimulus applied to the skin, without directly involving the mass of the muscle, evokes the reflex contraction of the muscle. Such a reflex is neither a muscle stretch reflex nor muscle-muscle reflex but a skin-muscle reflex. It is not a direct, but an indirect, muscle reflex; it is not intrinsic but extrinsic, or one might say "referred." It is not always local, and may be distant. The superficial reflexes differ from the deep reflexes in that they are evoked by a greater variety of stimuli; their "reflexogenous zones" are much more extended; their latent period is longer and is dependent entirely on the strength of the stimuli, and on their summation; their fatigability is greater. Whereas every muscle has its deep muscle reflex, only a few muscles have their superficial reflexes as well.

METHODS OF REENFORCEMENT

Of all the problems of the technic of reflex elicitation, only the methods of so-called reenforcement will be discussed here. The goal of these methods is to make a slight reflex more apparent and one seemingly lost perceptible. It is a common mistake to regard the reflex as lost when it is not. The methods of reenforcement which bring the reflex to light often help to avoid this error, with all its momentous diagnostic implications.

The deep reflex is a delicate and sensitive mechanism and is highly susceptible to the slightest external influence. Suffice it to mention that the tabetic patient who shows no reflexes when sober may manifest them while under the influence of alcohol, and that the knee jerk, for instance, increases the moment the patient falls asleep and decreases when he is in deep sleep (Ferguson[15]). The methods which facilitate the appearance of the deep reflexes are numerous and varied. Feix[16] and Trepiccioni[17] found that the best position for the patient during examination for deep reflexes was that in which he lay on his side, with legs bent at the hip and at the knee joints. If no response was obtained, the following means might be employed: better support of the limb, change of position, repeated passive movement and increased stretching of the muscles in question. The muscles may be struck, in preparation, by a hammer or be mildly massaged. When the patient keeps his muscles tense, the muscle stretch reflex can hardly be perceived; therefore the patient should be instructed to relax. Different methods may be used to distract his attention: He may carry on a conversation, look at a picture or stare at the ceiling, count, compute small sums, read aloud and fast, repeat the Lord's prayer or listen to music. Or the eyes may be examined simultaneously. Some investigators recommend slight sensory stimuli, such as a needle prick, a light flashed in the eyes, a cold or warm bath, massage or diathermy. For reenforcement of the knee jerk Plesch[18] used transverse compression of the patella and the tendon of the quadriceps muscle and the pinching of a fold of skin above the patella. Saggese[19] recommended quick pressure on the larynx and the upper part of the trachea from both sides, the thumb and index finger being used. Schreiber[20] advocated mild mas-

15. Ferguson, J.: Some Additional Remarks on Knee-Jerk, M. Rec. **4**:267, 1893.

16. Feix, J.: Ueber ein neues Verfahren zur Untersuchung des Patellar- und Achillessehnenreflexes, Wien. klin. Wchnschr. **19**:1223, 1906.

17. Trepiccioni, E.: Una nuova maniera di provocare il riflesso rotuleo, Policlinico (sez. prat.) **38**:6, 1931.

18. Plesch, J.: Handgriff zur leichten Auslösung des Kniesehnenreflexes, München. med. Wchnschr. **70**:637, 1923.

19. Saggese, V.: Una manovra per esaltare in particolari casi il riflesso patellare, Riv. di clin. pediat. **32**: 1159, 1934.

20. Schreiber, J.: Ueber das Knie-Phänomen, Deutsches Arch. f. klin. Med. **35**:254, 1884.

sage of the forelimb and repeated tapping of the tendon. Various other sensory stimuli have been recommended. Electrical stimulation was used by Knapp,[21] Boettiger [22] and Lewandowsky and Neuhof [23]; vibration was employed by Stscherback.[24]

Some maneuvers for reenforcement of the deep reflexes consist of active, forcible innervation of remote muscles on the part of the patient. Jendrassik,[25] in his famous method, recommended examination of the knee jerk at the moment the patient pulls his hooked hands apart. Laufenhauer, cited by Pándy,[26] asked the patient to squeeze the upper part of the physician's arm; Schoenborn [27] had him squeeze the examiner's left hand. The method of Krönig [28] requires the patient to draw in his breath deeply and quickly. Popper [29] and Marcus [30] suggested coughing and Kroner [31] recommended a short walk. Montemezzo [32] requested that the patient forcibly bend his trunk. Jendrassik,[33] and later Justman [34] and Weatherby,[35] recommended that the patient press down the thigh during examination for the knee jerk. They assumed that during this act the innervation of the antagonists would decrease the tonus of the quadriceps muscle. Faulkner,[36] on the same assumption, recommended that the patient, while lying in a supine position, press his heels against the bed. Balaban [37] requested the patient to press the ball of the foot against the left hand of the examiner. On the basis of the examination of 1,150 patients, Kostin [38] found that the patellar reflex can be elicited by the method of Balaban more easily than by any other means. Grinker [39] stated:

> An excellent method to obtain reinforcement of the knee jerk is to have the subject, with knees slightly flexed, gently press the ball of his foot against the examiner's free hand.

Krueger [40] let the patient hang his legs over the edge of the table, the calf resting against the edge, so that a 45 degree angle was formed. Here the weight of the legs has the same effect as the pressing down of the heel. The methods of Salomon [41] and Stevenson [42] consisted in active plantar flexion of the foot and toes; the method of Weidlinger,[43] in active lifting of the heel. Shvetzow [44] recommended tapping of the ligamentum patellae at the same moment that the patient makes an active dorsiflexion of the homolateral foot. The procedure of Negro [45] is similar: The patient, his heel placed on the floor, dorsiflexes his foot, and the examiner simultaneously exerts pressure on the thigh. The procedure, according to Negro, is intended to increase the tonus in the quadriceps muscle.

The explanation for the effectiveness of all these maneuvers is that they divert the attention of the patient. This helps him to relax the muscles he may have held in high tension, so

21. Knapp, A.: Kniephänomene und ein neuer Kunstgriff zu ihrer Auslösung bei multipler Neuritis (Pseudotabes polyneuritica), München. med. Wchnschr. **87**:749, 1940.

22. Boettiger, A.: Ein neues Hilfsmittel zum Nachweise schwächster Sehnenreflexe, Neurol. Centralbl. **29**: 122, 1910.

23. Lewandowsky, M., and Neuhof, H.: Ueber Wiederbelebung der Reflexe, Ztschr. f. d. ges. Neurol. u. Psychiat. **13**:444, 1912.

24. Stscherback, cited by Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1910, vol. 1, p. 587.

25. Jendrassik, E.: Zur Untersuchungsmethode des Kniephänomens, Neurol. Centralbl. **4**:412, 1885.

26. Pándy, K.: Die Kraft der Sehnenreflexe und die Veränderung derselben bei der Hemiplegie, Neurol. Centralbl. **23**:449, 1904.

27. Schoenborn, S.: Bemerkungen zur klinischen Beobachtung der Haut- und Sehnenreflexe, Deutsche Ztschr. f. Nervenh. **21**:273, 1902.

28. Krönig, G.: Ein einfacher Kunstgriff zur Erzeugung des Kniephänomens, Berl. klin. Wchnschr. **43**: 1421, 1906.

29. Popper, E.: Zur Kenntnis des Patellarreflexes, Deutsche Ztschr. f. Nervenh. **67**:131, 1920.

30. Marcus, I. H.: Coughing: A Method of Reenforcing the Knee Jerk Reflex, Arch. Neurol. & Psychiat. **34**:1295 (Dec.) 1935.

31. Kroner, cited by Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1910, vol. 1, p. 587.

32. Montemezzo, A.: Sul reflesso rotuleo: semplice espediente a facilitarne il rilievo, Scritti di sc. med., 1923, p. 239.

33. Jendrassik, E.: Beiträge zur Lehre von den Sehnenreflexen, Deutsches Arch. f. klin. Med. **33**:177, 1883.

34. Justman, S.: Sur une nouvelle méthode pour obtenir le réflexe rotulien, Rev. neurol. **30**:225, 1923.

35. Weatherby, E.: The Justman Method of Eliciting the Knee-Jerk, Mil. Surgeon **89**:902, 1941.

36. Faulkner, J. M.: A Simple and Effective Method of Reenforcing the Knee Jerk, Arch. Neurol. & Psychiat. **28**:895 (Oct.) 1932.

37. Balaban, J. M.: Méthode d'exploration du réflexe rotulien, Arch. internat. de neurol. **56**:287, 1937.

38. Kostin, A.: Examination of the Patellar Reflexes by the Method of Dr. Balaban, Sovet. nevropat. **4**:170, 1935.

39. Grinker, R., in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1925, vol. 9, p. 259.

40. Krueger, E.: Zur Erleichterung von Reflexprüfungen, München. med. Wchnschr. **2**:1273, 1939.

41. Salomon, E.: Eine zweckmässige Art den Patellarreflex auszulösen, Neurol. Centralbl. **30**:80, 1911.

42. Stevenson, F. E.: Reenforcement of the Knee Jerk in Children, Arch. Neurol. & Psychiat. **31**:614 (March) 1934.

43. Weidlinger, E.: Empfindliche Methode zur Auslösung des Patellarreflexes, Med. Klin. **29**:847, 1933.

44. Shvetzow, S. P.: On the Mechanism of Artificial Stimulation of the Knee Jerk, Sovet. nevropat., psikhiat. i psikhogig. **1**:591, 1932.

45. Negro, C.: Di una particolare modalità tecnica di esplorazione del fenomeno del ginocchio, Gior. di med. mil. **69**:598, 1921.

that the appearance of the reflex is facilitated. Further, it is thought that active innervation of antagonist muscles serves to bring about a reflexive relaxation in the muscles in question. While this is true, observers, on the other hand, have come increasingly to realize that without a certain tension in the muscles in question no reflex will appear. The efficiency of some of the described maneuvers has therefore been sought in the fact that active innervation of neighboring, antagonistic or remote muscles brings about a slight, involuntary increase in the tension of the muscles in question, which results from an overflowing of the impulse. This increase of muscle tension facilitates the work of the reflex mechanism, increases the strength of the reflex or allows it to appear at all.

Another point is worth mention. In patients with lesions of the pyramidal tract, associated movements appear in the affected limbs on voluntary muscular effort of any kind. These associated movements, for instance those in the leg, are similar to movements which may be produced by elicitation of the knee or ankle jerk. It is thus conceivable that through effort of any kind these associated movements appear in mild or subclinical form. They support the reflexive movement, since the results of the two types are the same; in the leg, for instance, they both produce extension.

Another neglected point in the discussion of the effectiveness of the aforementioned maneuvers may be briefly considered here. From clinical experience and from experiments (Montgomery and Luckhardt [46]), it is known that pronounced increase of intracranial pressure brings about prompt diminution or abolition of the knee jerk. Aird [47] showed, however, that a slight increase of intracranial pressure, such as that produced by prolonged jugular compression, will make the deep reflexes more apparent. Since some of the maneuvers mentioned for reenforcement of the deep reflexes, such as pulling the hooked hands apart, coughing or bending the trunk, are accompanied by notable increase in intracranial pressure, it is quite justifiable to assume that this increased pressure may contribute to the appearance and augmentation of the reflexes.

On the basis of his studies of action currents of the muscles, Hoffmann [48] stressed that complete voluntary relaxation of the muscles diminishes the characteristic action currents which normally appear with deep reflexes. Conversely, the action currents of the deep reflexes increase during voluntary contraction of the muscles. Weber [49] recently proved that this is true also for the masseter reflex. The simultaneous, voluntary innervation of the muscle through which the reflex is carried opens the gateway for this reflex. Weber observed that when the innervation of the muscles in question is lessened, the reflex decreases, and that it finally disappears when the antagonistic muscles are innervated. On the basis of these observations on sensitization of the reflex through mild active innervation of the muscles in question, Hoffmann recommended slight voluntary innervation of the corresponding muscles for reenforcement of the deep reflexes. In accordance with this view, von Weizsäcker [50] explained the efficiency of the maneuvers of Jendrassik and others in the following way: Through such a maneuver, a muscle which has been overly tense becomes less tense; on the other hand, a completely relaxed muscle receives overflowing impulses from remote muscles which are actively innervated. This facilitates the elicitation of the reflex. On the basis of physiologic experiments with the patellar reflex, Sommer [51] concluded that with the maneuver of Jendrassik a stimulus is reflexly transmitted from the excessively innervated muscle groups to the quadriceps muscle. This stimulation acts in the same way as stretching of the whole muscle and thus increases the susceptibility of the quadriceps muscle to further, passive stretching. In this connection, it is worthy of note that in case of hysteria, with complete muscular relaxation, the deep reflexes may transiently be absent (Nonne [52] and Wohlwill [53]). They may even be diminished under the influence of rest or mere ideas of sleep (Karger [54]). It was found in physiologic experi-

46. Montgomery, M. F., and Luckhardt, A. B.: Studies on the Knee Jerk: VIII. The Effects of Acutely Raised Intracranial and Intraspinal Pressures upon Knee Jerk, Am. J. Physiol. **91**:210, 1929.

47. Aird, R. B.: Prolonged Jugular Compression, Arch. Neurol. & Psychiat. **45**:633 (April) 1941.

48. Hoffmann, P.: Die physiologischen Eigenschaften der Eigenreflexe, Ergebn. d. Physiol. **36**:15, 1934.

49. Weber, W.: Physiologische Untersuchungen über den Masseterreflex beim Menschen, Deutsche Ztschr. f. Nervenh. **144**:160, 1937.

50. von Weizsäcker, V.: Neuere Forschungen und Anschauungen über Reflexe und ihre physiologische Bedeutung, Klin. Wchnschr. **1**:2217, 1922.

51. Sommer, J.: Periphere Bahnung von Muskeleigenreflexen als Wesen des Jendrassikschen Phänomens, Deutsche Ztschr. f. Nervenh. **150**:249, 1940.

52. Nonne, M.: Zwei durch zeitweiliges Fehlen des Patellarreflexes ausgezeichnete Fälle von Hysterie, Deutsche Ztschr. f. Nervenh. **24**:474, 1903.

53. Wohlwill, F.: Ueber funktionell bedingtes Fehlen der Patellarreflexe, Neurol. Centralbl. **28**:567, 1909.

54. Karger, P.: Reflex, Wille und Vorstellung, Klin. Wchnschr. **3**:2273, 1924.

ments (Jacobson and Carlson [55]) that the knee jerk decreases constantly with progress in relaxation and that in some subjects a degree of relaxation could be obtained in which the knee jerk was abolished without the subject's going to sleep. All this demonstrates clearly the influence of active innervation of the muscles on the so-called tendon reflexes.

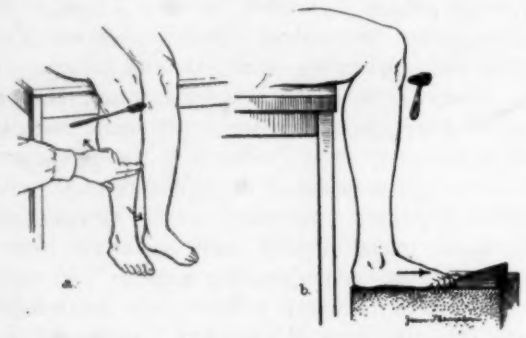

Fig. 1.—Method of reenforcement of the patellar reflex by active innervation of the quadriceps muscle. (*a*) The patient pushes his leg slightly forward; the examiner opposes this movement with his left hand and simultaneously strikes the patellar tendon with the hammer held in the right hand. (*b*) The patellar tendon is struck by the examiner while the patient pushes his foot against resistance offered by the perpendicular surface of the block on the footstool.

Sträussler [56] stated that he tapped the patellar tendon immediately after a brisk, passive bending at the knee. This maneuver increases the innervation of the quadriceps muscle, increases its tension and thus facilitates the elicitation of the patellar reflex.

From all these observations an important and workable maneuver for the reenforcement of the deep reflexes results. When a reflex is being elicited, a slight voluntary contraction of the muscles involved in this reflex must take place. The invisible reflex may then become visible and the weak one appear stronger. The practical procedure for facilitation of the appearance of the patellar reflex, for instance, is as follows: The patient sits on a table, his legs hanging loosely; he is asked to push one foot slightly forward against the resistance of the fingers of the examiner, who thus can appraise and control the amount of pressure exerted by the patient. This control is important because the innervation of the quadriceps muscle must be very slight. A strong effort on the part of the patient may not facilitate the elicitation of the reflex; on the contrary, it may interfere with its appearance. The moment the patient innervates the quadriceps muscle, the patellar tendon is tapped and the reflex elicited (fig. 1 *a*). Another method is to ask the patient, while sitting on the table, with his feet resting flat on the footstool, to push his foot slightly against the perpendicular surface of the block which extends across the footstool (fig. 1 *b*). For elicitation of the achilles reflex, the patient is asked to push the ball of his foot slightly downward, so that the calf muscles are innervated; the examiner opposes this movement with his hand and so controls the pressure exerted by the patient. The achilles tendon is tapped the moment the patient presses his foot down (fig. 2 *a*). Or the patient, sitting on the table, with his foot resting on the footstool and the ball of the foot placed on the angular surface of a block on the footstool, is asked to push the ball of his foot down slightly (fig. 2 *b*). Similar procedures may be used for elicitation of other reflexes. The effect of a slight, active flexion of the fingers on the reenforcement or appearance of the finger flexor reflex is particularly striking. In my experience the method of increased innervation has undoubtedly been the best means of elicitation and reenforcement of the deep reflexes. No deep reflexes should be declared as lost unless this method has been tried (Roemheld [57]).

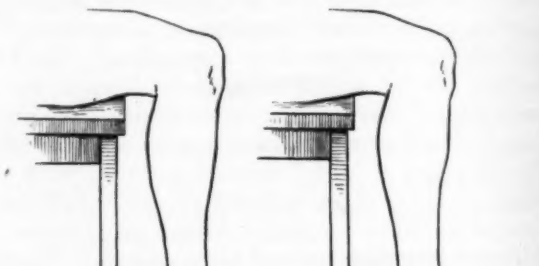

Fig. 2.—Method of reenforcement of the achilles reflex. (*a*) The patient, sitting on the table with the legs hanging loosely, pushes down the ball of the foot slightly against the hand of the examiner while the latter strikes the achilles tendon with the hammer. (*b*) The achilles tendon is struck by the examiner while the patient presses the ball of the foot against the angular surface of the block on the footstool.

I shall now consider individually some of the clinically most important reflexes.

55. Jacobson, E., and Carlson, A.: The Influence of Relaxation upon the Knee-Jerk, Am. J. Physiol. **73**: 324, 1925.

56. Sträussler, E.: Ein einfacher Kunstgriff zur Auslösung schwer auslösbarer Patellarreflexe, Wien. med. Wchnschr. **82**:398, 1932.

57. Roemheld, L.: Ueber die Auslösung der Eigenreflexe und ihre Bedeutung, Deutsche med. Wchnschr. **64**:46, 1938.

ORBICULARIS OCULI REFLEX

The orbicularis oculi muscle protects by contraction the bulbus oculi and the retina from external noxious influences. The mechanism of its reflex action is especially elaborate and shows peculiarities which other muscles do not possess. The threshold for reflexive contraction is extremely low. The reaction of the muscle is rapid—so rapid that in every language there is the expression "quick as a wink." The reaction is bilateral. A further outstanding characteristic of the reflex mechanism of this muscle is the great variety of stimuli which bring it into play. The orbicularis oculi muscle contracts reflexly on stimulation of the cochlea, the phenomenon being known as the cochleopalpebral reflex, or the auropalpebral or acousticopalpebral reflex. This reaction is strikingly manifested when the patient is startled by an unexpected sound, such as a pistol shot (Strauss, Landis and Hunt [58]). The muscle contracts also on visual stimuli, when an object or light is suddenly brought into the field of vision; this is the old visual orbicularis reflex of Descartes, also called the wink reflex, or the opticofacial reflex (Borowsky [59]).

Imperatori [60] recently described a palatopalpebral reflex, in which the eye closes when the palate is touched. Gallenga [61] observed in dogs, either normal or decerebrated, a reflex contraction of the orbicularis oculi muscle on stimulation of the superior laryngeal nerve. The extreme delicacy and responsiveness of the highly efficient reflex mechanism of the orbicularis oculi muscle may be demonstrated in other ways (Galant [62]). It may be compared with the cough reflex. This, too, may be elicited in many ways. The orbicularis oculi muscle has its skin-muscle reflex—the corneal reflex may be regarded as such. One may assume that this muscle has also its own muscle reflex, which is evoked by direct concussion and stretching of the muscle substance. This response, which should be called the orbicularis oculi reflex, can be elicited by tapping the muscle directly or by tapping the neighboring bones—the front of the head, the temporal area or the bone and cartilages of the nose. Since, as has been seen, the threshold of a reflex contraction of the orbicularis oculi muscle is extremely low, it is understandable that the slightest concussion of the bone on the surface of which the muscle directly lies may, by transmission of the concussion to the muscle, evoke its contraction. The fibers of the orbicularis oculi muscles are intimately interwoven with each other and with the surrounding muscles of the face. They represent an anatomic continuity which makes them a physiologic unity. Thus, the slightest concussion of the neighboring muscles is easily transmitted to the homolateral and to the heterolateral orbicularis oculi muscle. Weisenburg [63] stated:

> The normal reflex [of the orbicularis oculi muscle] is obtained by tapping over the frontal region as far as the border of the hair, the exaggerated form by tapping as far back as the vertex, and the diminished form can only be obtained by tapping directly over the supra-orbital nerve.

With this one may agree, except that it is the tapping of the muscle or the bone, and not the supraorbital nerve, that constitutes the essential stimulus. The nearer the point of stimulation is to the muscle, the stronger is the reflex.

The orbicularis oculi muscle, especially its lower part, reacts so easily to such a multitude of external stimuli that on tapping either this muscle or its neighboring area one runs the danger of eliciting a reflex of a different order, of affecting the muscle through means other than concussion and stretching. Care must be taken to avoid as far as possible these other stimuli. It is of course impossible to avoid them completely. With careful technic, however, one has a definite impression that the element of direct concussion and stretching of the muscles in elicitation of the reflex is so dominant that, whereas other stimuli are capable of producing the reflex, they do not enter into practical consideration.

By the following technic (fig. 3), for instance, one avoids to a maximal degree every stimulus other than stretching, i. e., visual or auditory stimuli, startling, gross irritation of the skin in any form and stimuli to the periosteum or bone. The examiner holds a fold of skin between his thumb and index finger at the outer corner of the eye, at the temple, pulling it slightly backward so as to stretch the orbicularis oculi muscle mildly. The examiner then taps his thumb lightly with the reflex hammer, or with a finger of the other hand, and evokes a sudden additional stretching of the muscle. A reflex contraction of the orbicularis oculi muscle follows on this side and, to a milder degree, on the other

58. Strauss, H.; Landis, C., and Hunt, W. A.: Acoustic Motor Reactions, Arch. Otolaryng. **28**:941 (Dec.) 1938.

59. Borowsky, M. L.: Der Blinzelabwehrreflex, usw., Deutsche Ztschr. f. Nervenh. **110**:134, 1929.

60. Imperatori, C. J.: The Palatal Palpebral Reflex, M. J. & Rec. **131**:198, 1930.

61. Gallenga, R.: Sopra un riflesso palpebrale, Ateneo parmense **1**:585, 1929.

62. Galant, J. S.: Die Lidreflexe, Arch. f. Kinderh. **74**:130, 1924; Die Blinzelreflexe und einige andere Lidphänomene, ibid. **75**:37, 1925.

63. Weisenburg, T. H.: A Consideration of the Facial Reflexes and Nerve and Muscle Phenomena in the Distribution of the Fifth and Seventh Nerves, Univ. Pennsylvania M. Bull. **16**:63, 1903-1904.

side, exactly in proportion to the strength of the tapping. Here it is evident that the orbicularis oculi muscle contracts reflexly, as is the case with all other muscles on sudden passive stretching of the muscle fibers themselves. The response, then, is a true deep muscle reflex, a muscle-muscle reflex. The assumption that the orbicularis oculi muscle has a deep muscle reflex of its own is based on purely clinical observation. To this opinion I adhere, despite the fact that Sommer,[64] a pupil of Hoffmann, on examination of the electric currents of the muscle, concluded that the mimic muscles of the face have no deep reflexes, no *Eigenreflexe,* according to the terminology of Hoffmann. Long before him, Sternberg [8] asserted that no "tendon reflexes" existed in the facial muscles.

The reflex appearing on concussion and stretching of the orbicularis oculi muscle is a normal phenomenon, and its strength varies

Fig. 3.—Method of elicitation of the orbicularis oculi reflex. The examiner holds a fold of skin over the temple between his thumb and index finger; he pulls slightly backward and strikes his thumb lightly with the hammer or his finger, thus causing additional stretching of the orbicularis oculi muscle.

greatly in different persons, as is the case with every other deep muscle reflex. One cannot subscribe to Foerster's [65] statement that this reflex is inconstant. Its constancy was emphasized in special studies of Zeri,[66] Kartschikjan [67] and Weingrow.[68] Weingrow called it "a true and absolutely constant reflex," and with him I agree. The reflex is also constant in apes (Aronovitch [69]). The greatest diagnostic importance of this reflex lies in the fact that its diminution indicates a facial palsy of peripheral type and that the degree of this diminution parallels that of the palsy. In a case of facial palsy of central type the reflex is either preserved or exaggerated (Bickel [70] and Glattauer [71]). Of physiologic interest is the exaggeration of this reflex in cases of postencephalitic parkinsonism (Zylberlast-Zand; [72] Guillain, Alajouanine and Marquézy [73]). This exaggeration is so constant that it must be regarded as a definite sign of parkinsonism.

This reflex is usually classified as a superficial, or cutaneous, reflex. Overend [74] expressed the opinion that it was "a true skin reflex and not a periosteal reaction." Von Bechterew,[75] Foerster [76] and Monrad-Krohn [77] saw in it a periosteal reflex. Guillain [78] called it a cutaneous and periosteal reflex. Simchowicz [79] spoke of a perichondrial reflex which may be transformed into a periosteal one. Lewandowsky [80] called it a bone reflex. Kornilow [81] expressed the belief that this reflex was neither cutaneous nor periosteal, but that it belonged to the "defense reflexes." Böhme [82] saw in it a protective reflex

64. Sommer, J.: Hat die mimische Gesichtsmuskulatur Eigenreflexe oder nicht? Deutsche Ztschr. f. Nervenh. **146**:294, 1938.

65. Foerster, O., in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 6, p. 238.

66. Zeri, A.: Du réflexe trigémino-facial ou trigéminoorbiculaire des paupières, Ann. d. Ist. sichiat. d. r. Univ. di Roma **3**:269, 1904; abstracted, Rev. neurol. **14**:15, 1906.

67. Kartschikjan, S.: Motor Reaction of the Face Muscles on Mechanical Stimulation, Obozr. psikhiat., nevrol. **2**:175, 1922.

68. Weingrow, S. M.: Facial Reflexes, Arch. Pediat. **50**:234, 1933.

69. Aronovitch, G. D.: Reflexes in Apes, J. Nerv. & Ment. Dis. **65**:457, 1927.

70. Bickel, A.: Die klinische Bedeutung der Knochenreflexe, Charité-Ann. **36**:186, 1912.

71. Glattauer, A.: Zur Physiopathologie und Klinik des Nasenrückenlidreflexes, Schweiz. Arch. f. Neurol. u. Psychiat. **44**:243, 1939.

72. Zylberlast-Zand, N.: Le réflexe oculo-palpébral chez les parkinsoniens postencéphalitiques, Rev. neurol. **39**:102, 1923.

73. Guillain, G.; Alajouanine, T., and Marquézy, R.: L'exagération du réflexe naso-palpébral dans les syndromes post-éncephalitiques, Compt. rend. Soc. de biol. **91**:364, 1924.

74. Overend, W.: Preliminary Note on a New Cranial Reflex, Lancet **1**:619, 1896.

75. von Bechterew, W.: Ueber Reflexe im Antlitz- und Kopfgebiete, Neurol. Centralbl. **20**:930, 1901.

76. Foerster,[65] p. 239.

77. Monrad-Krohn, G. H.: The Clinical Examination of the Nervous System, ed. 7, New York, Harper & Bros., 1938, p. 126.

78. Guillain, G.: Le réflexe naso-palpébral (réflexe trijumeau-facial) et sa valeur pronostique dans la paralysie faciale, Compt. rend. Soc. de biol. **83**:1394, 1920.

79. Simchowicz, T.: Ueber den Nasenaugenreflex und den Nasenkinnreflex, Deutsche Ztschr. f. Nervenh. **75**:343, 1922.

80. Lewandowsky, M., in Handbuch der Neurologie, Berlin, Julius Springer, 1910, vol. 1, p. 584.

81. Kornilow, A.: Ueber cerebrale und spinale Reflexe, Deutsche Ztschr. f. Nervenh. **23**:216, 1903.

82. Böhme, A., in Bethe, A.; Bergmann, G., and others: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10, p. 982.

of the eye. Moro [83] observed that this reflex was constant in the newborn and in infants on tapping of the forehead, and occasionally the dorsum or the tip of the nose. This reflex did not appear on the tapping of other points. This speaks, according to Moro, against the simple protective nature of the reflex. My view of the nature of this important reflex may be summarized as follows: The threshold for reflex action of the orbicularis oculi muscle is extremely low. Its contraction may be effected, as has been seen, through multitudinous stimuli, and application of a single stimulus is certainly difficult. Nevertheless, with careful technic one has a definite impression that other stimuli are reduced to a minimum and that concussion and stretching alone are effective. It is therefore justifiable to assume that the orbicularis oculi muscle has its own deep muscle reflex, as have all other muscles. It is the painstaking observation on the technic of elicitation that teaches one unmistakably the nature of this reflex, that of a true muscle stretch reflex.

This reflex has a long history. It was first described by Overend [74] in 1896 as "a new cranial reflex," or "frontal reflex." He elicited the phenomenon by gently tapping the forehead. He also noticed that a tap on the middle line of the forehead was followed by twitchings on both sides. This reflex is usually named after McCarthy,[84] who in 1901 described it as a "supraorbital reflex." He attributed what he called "fibrillary tremor, but not contraction," of the orbicularis oculi muscle to the tapping of the supraorbital nerve. Under the name "ocular reflex," von Bechterew [85] described the same phenomenon: contraction of the orbicularis oculi muscle when any point over the frontotemporal or zygomatic area of the skull was tapped. In disagreement with McCarthy, he emphasized that one is dealing here with a contraction of the muscle and that this can be achieved in other ways than by taping the supraorbital nerve. Weisenburg,[63] in 1903 spoke of "the ophthalmic, or supra-orbital, reflex." In 1904 this reflex was again described by Zeri [66] as the trigeminofacial, or the trigemino-orbicular, reflex, and in 1907 it was described by Mondino.[86] In 1920 Guillain [78] described a "nasopalpebral reflex," which was elicited by percussion at the root of the nose. This is not a "variant" of the McCarthy reflex, as it is often called, but is the same reflex. Eighteen years before Guillain, von Bechterew [85a] stressed that this reflex can be elicited over the whole area of the frontal muscle. Since the value of this reflex lies essentially in the comparative strength of the contractions of the orbicularis oculi muscle on the two sides, the most practical point of elicitation is the glabella; however, there is no use in proposing a new name, "glabella reflex," as I [87] did in 1930. Physiologically and didactically it is more correct to name the reflex according to the muscle involved than according to the point of its elicitation. In 1922 Simchowicz [79] described the same reflex under the name "nose-eye reflex." He elicited this reflex by tapping the tip of the nose, as Moro [83] had done long before him. In some cases he found a very weak, hardly perceptible contraction of the lower lid. It is easily understandable that when the nose is tapped the provoked concussion of the underlying cartilage and bones can be transmitted to the orbicularis oculi muscles, the threshold of stimulation of which is very low. Simchowicz expressed the opinion that the reflexes of von Bechterew, McCarthy and Zeri are "closely related." They are, in fact, completely identical. According to Simchowicz, his reflex is "the first example of a perichondrial reflex." He interpreted the fact that the reflex can be elicited not only from the bridge of the nose as far as the glabella but from the frontal bone as "a transformation of a perichondrial reflex into a periosteal." Glattauer,[71] too, spoke of a periosteal-perichondrial reflex. But there is as little evidence of the existence of perichondrial as of periosteal reflexes. It is more logical to assume that every concussion of neighboring structures, whether of the nose or of the frontal bone, is easily transmitted to the orbicularis oculi muscles, where it readily provokes a contraction.

In a search for new reflexes, Galant,[88] in 1926, described a "cephalopalpebral reflex" consisting of contraction of the orbicularis oculi muscle, chiefly of the lower lid, when the top of the skull

83. Moro, E.: Ueber Gesichtsreflexe bei Säuglingen, Wien. klin. Wchnschr. **19**:637, 1906.

84. McCarthy, D. J.: Der Supraorbitalreflex, Neurol. Centralbl. **20**:800, 1901; Weiteres zur Kenntnis des Supraorbitalreflexes, ibid. **21**:843, 1902.

85. von Bechterew, W.: (*a*) Ueber den Augenreflex oder das Augenphänomen, Neurol. Centralbl. **21**:107, 1902; (*b*) Ueber den Zustand der Muskel- und sonstigen Reflexe des Antlitzes bei Dementia paralytica, ibid. **22**:850, 1903; (*c*) footnote 75.

86. Mondino, C.: Di uno speciale riflesso che si osserva nella contrattura facciale, Riv. di pat. nerv. **12**:49, 1907; abstracted, Neurol. Centralbl. **26**:855, 1907.

87. Wartenberg, R.: Kleine Hilfsmittel der neurologischen Diagnostik, Nervenarzt **3**:594, 1930.

88. Galant, J. S.: Der cephalopalpebrale Reflex (CPR), der cephalopalpebro-nasale Reflex (CPNR) und ihnen verwandte Reflexe, die vom schädeldach ausgelöst werden, Psychiat.-neurol. Wchnschr. **28**:490, 1926.

is tapped. He elicited this reflex in persons with neuroses of many kinds. This new term has no right to existence, since the reflex is apparently only an orbicularis oculi reflex elicited by concussion of the frontal bone. Here the reflex is elicited from a slightly more distant point. Elicitation of this response is possible in persons with increased general reflex irritability, which includes the normally extremely susceptible orbicularis oculi muscle. It is possible that this reflex is a startle action, the threshold of which is very low in neurotic persons. The latest publication on this subject appeared in 1939, in which Glattauer [71] recommended the name "nose-bridge-lid reflex."

The chaos of nomenclature concerned with this reflex is best illustrated by the following statement in a paper published in 1937, describing the neurologic status in a case: "supraorbital, nasopalpebral, glabella reflexes preserved." These three names, like all others—for instance, nose-bone reflex, eye closure reflex, eye reflex, nose-eye reflex, trigeminofacial reflex and trigemino-orbicular reflex—should be replaced by the simple, physiologically correct name "orbicularis oculi reflex." It is the muscle, not the bones, the skin, the periosteum or the perichondrium, which is at the root of this phenomenon.

JAW REFLEX

When the muscles which elevate the lower jaw and close the mouth are subjected to a brisk stretching, they contract and the lower jaw moves briskly upward. This constitutes the jaw reflex, usually called the masseter reflex. This name is not quite correct, since in closing the mouth, not only the masseter but the temporal muscles are involved. Although mentioned by Fuller [89] in 1884, this reflex was first described in 1886 by de Watteville.[90] who called it the jaw jerk, or the masseteric tendon reaction. Von Bechterew [75] called it the mandibular reflex.[29] Since this reflex is practically the only one concerned with the jaw, it is appropriately called the jaw reflex, as Dana [91] did. The sudden stretching of the muscles which close the mouth may be accomplished in various ways. The front of the chin may be tapped directly with the reflex hammer; the thumb may be placed on the chin and tapped, or a tongue blade may be placed on the lower teeth and tapped. Jendrassik [92] could elicit this reflex easily, also, by tapping the lower surface of the zygomatic arch at the point of insertion of the masseter muscle. As was pointed out previously,[93] this reflex can easily be elicited also by tapping a tongue blade placed on the root of the tongue, without touching the teeth. The exaggeration of the reflex is more conspicuous, and the reflex appears on milder stimuli, with this technic than with direct tapping of the lower jaw. This reflex may be increased, even to a state of clonus of the lower jaw, in cases of bilateral suprapontile cerebral lesions, for instance pseudobulbar palsy.[94] This association was first described by Beevor.[95] It is worthy of note that the jaw reflex may be exaggerated without proper "pseudoparalytic" signs, the localization of the lesion being the decisive factor. The clinical value of this reflex is generally slight. Curschmann [96] pointed out that the behavior of the jaw reflex may be of value in the differential diagnosis of hyporeflexia and areflexia on a constitutional basis or on the basis of a local lesion. If not only the reflexes of the muscles of the limbs but the jaw reflex is absent, the areflexia is probably constitutional. If the jaw reflex is preserved and the reflexes of the limbs are lost, a local pathologic process is probably at work.

HEAD RETRACTION REFLEX

The muscles of the back of the neck, the retractors of the head, have a deep muscle reflex of their own. This reflex was described in detail in a previous paper (Wartenberg [97]). To elicit this reflex one evokes a quick, sharp bending of the head. This is best achieved by sharply tapping the maxillary bone beneath the nose while the head is slightly bent. If a brisk, quick, involuntary backward jerk of the head takes place, the reflex is said to be positive. If only a slight concussion of the whole head results from the tap, the reflex is absent. This reflex

89. Fuller, S. E.: Pseudo-Bulbar Paralysis, M. Rec. **26**:487, 1884.

90. de Watteville, A.: Note, Brain **8**:518, 1886.

91. Dana, C. L.: Text-Book of Nervous Diseases, ed. 10, Baltimore, William Wood & Company, 1925, p. 57.

92. Jendrassik, E.: Ueber die allgemeine Localisation der Reflexe, Deutsches Arch. f. klin. Med. **52**:574, 1894.

93. Wartenberg, R.: Zur Klinik und Pathogenese der Pseudobulbärparalyse, Monatschr. f. Psychiat. u. Neurol. **51**:251, 1922.

94. The textbooks use the time-honored, but misleading, term "pseudobulbar palsy." To distinguish the two types of bulbar palsy, the nuclear and the supranuclear, the term "flaccid bulbar palsy" and "spastic bulbar palsy" are preferable.

95. Beevor, C. E.: A Case of Amyotrophic Lateral Sclerosis with Clonus of the Lower Jaw, Brain **8**:516, 1886.

96. Curschmann, H.: Ueber konstitutionelle Hypo- und Areflexie, Deutsche Ztschr. f. Nervenh. **83**:51, 1925.

97. Wartenberg, R.: Head Retraction Reflex, Am. J. M. Sc. **201**:553, 1941.

is usually not observed in normal persons but can be seen distinctly in patients with bilateral lesions of the pyramidal tracts which involve the nuclei of innervation of retractor muscles of the head. Though the evaluation of this reflex is sometimes difficult, a critical review of my own experience convinced me that this reflex may be of great, sometimes of decisive, help in the diagnosis of bilateral supracervical lesions of the pyramidal tract. The reflex is most clearly seen in cases of advanced amyotrophic lateral sclerosis, bilateral spastic paralysis and dorsolateral sclerosis.

FINGER FLEXOR REFLEX

The flexors of the fingers react like any other striated muscle: They contract on brisk stretch. This contraction constitutes the finger flexor reflex. There are numerous ways in which one may effect a sudden stretching of the finger flexors which will result in their contraction. The best method is as follows (fig. 4): The patient, his half-supinated hand resting with its dorsum on his knee, sits facing the examiner. The examiner places his middle and index fingers across the slightly bent tips of the patient's four fingers and taps his own fingers lightly with the percussion hammer. A flexion of the patient's four fingers, as well as of the end phalanx of the thumb, is felt and seen. This response constitutes the positive reflex. It is essential that the hand of the examiner be loose and that the blows of the hammer be dealt swiftly, briskly, abruptly and with maximal elasticity. The fingers should not be palpated, but should be struck suddenly.

The best method of reenforcing this reflex, that is, of making it appear at all if it is not perceptible or of making it more distinct, is to have the patient bend his fingers when the blow is applied. This method is effective and is highly recommended. It is essential of course that the active bending of the patient's fingers be slight. While many authors, for instance Perelman,[98] have stressed the importance of complete relaxation of the fingers on examination for Hoffmann's sign, I contend that the optimum position for this examination is a slight, active bending of the fingers.

It is often necessary to repeat the examination, and with varying force, while the patient's fingers are bent in different degrees and while the position of the hand is slightly changed. The direction of the blow of the percussion hammer may be modified, too. The reflex is "whimsical." The results of repeated tests may differ. By careful application of the aforementioned technic, by patient repetition of the examination and by delicate use of the method of reenforcement, one can elicit this reflex in normal persons in full, with flexion of all the fingers and of the thumb.

The finger flexor reflex must thus be regarded as a normal reflex. Of course its palpable, visible evidence varies greatly, as is true of many other reflexes. It is sometimes barely perceptible and often greatly diminished. It is occasionally elicited only through the method of reenforcement described. This is simply because, as Moore[99] pointed out, the normal tonus of the finger flexors varies notably in different persons. It must be stressed that the presence of the reflex does not constitute a sign of a lesion of the pyramidal tract. With such a lesion this reflex is distinct, but the reverse is not true: A greatly increased reflex does not in itself indicate a lesion of the pyramidal tract. In other words, a patient with a strongly positive finger flexor reflex *may* have a pyramidal lesion, but not necessarily. If this reflex is strongly positive or is exaggerated, one may, it is true, suspect the presence of a pyramidal lesion, but there is no definite way by which one may distinguish exaggeration of the finger flexor reflex due to functional hyperirritability and that due to a lesion of the pyramidal tract. The same

Fig. 4.—Method of elicitation of the finger flexor reflex. The patient bends the terminal phalanges of his fingers; the examiner places his middle and index fingers on the volar surface of the phalanges and strikes his own fingers with the hammer; reflex contraction of the patient's fingers can be seen and felt.

98. Perelman, I.: The Sign of Hoffmann and Its Clinical Importance, Sovet. nevropat. **4**:145, 1935.

99. Moore, R.: Reflex of the Upper Extremity, J. A. M. A. **65**:528 (Aug. 7) 1915.

is true of other reflexes, such as the patellar. That the finger flexor reflex may be barely perceptible in normal persons, or not perceptible at all, does not mean that when it is distinct it is indicative of a lesion of the pyramidal tract. Like many other reflexes, this reflex often exists in latent form.

This reflex, consisting of flexion of the fingers on tapping of their volar tips, is often called the "finger Rossolimo" sign. Foerster [100] called the "finger Rossolimo" sign, together with the Babinski and the "toe Rossolimo" sign, the fine diagnostic signs of a lesion of the pyramidal tract. Although this statement was made by no less a man than Foerster, one cannot subscribe completely to the assertion in this form, since it is misleading. The finger Rossolimo sign is in itself not a pyramidal sign. It may be considered pathologic only when it is highly exaggerated or appears unilaterally.

There are many ways by which one may stretch the flexor muscles of the fingers and elicit the finger flexor reflex. About 1900 Hoffmann introduced a method of elicitation of the reflex which has been known as Hoffmann's sign, Hoffmann's "reflex phenomenon," the "snapping reflex" or the "digital reflex." He never described the reflex; this was first done in 1911 by his pupil Curschmann.[101] This sign, interestingly, has a greater popularity in America than in Europe, or even in Germany. Several articles devoted to this sign have been published in the United States (Keyser,[102] Pitfield,[103] Fay and Gotten [104] and Echols [105]). Even a history of the Hoffmann sign has been written (Bendheim [106]). The technic of elicitation of this reflex is as follows: The examiner holds the middle phalanx of the patient's middle finger between his own second and third fingers and, with a sharp and forcible flick of his thumb, nips the nail of the patient's finger, thus flexing it and suddenly releasing it. The reflex is said to be positive when flexion of the other fingers, including the thumb, follows.

100. Foerster,[65] p. 244.

101. Curschmann, H.: Ueber die diagnostische Bedeutung des Babinskischen Phänomens im präurämischen Zustand, München. med. Wchnschr. **58**:2054, 1911.

102. Keyser, T. S.: Hoffmann's Sign or the "Digital Reflex," J. Nerv. & Ment. Dis. **44**:51, 1916.

103. Pitfield, R. L.: The Hoffmann Reflex: A Simple Way of Reinforcing It and Other Reflexes, J. Nerv. & Ment. Dis. **69**:252, 1929.

104. Ray, T., and Gotten, H.: Clinical Observations on the Value of the Hoffmann Sign, J. Nev. & Ment. Dis. **77**:594, 1933.

105. Echols, D.: The Hoffmann Sign, J. Nerv. & Ment. Dis. **84**:427, 1936.

106. Bendheim, O. L.: On the History of Hoffmann's Sign, Bull. Inst. Hist. Med. **5**:684, 1937.

There is little in the literature on the physiology of this phenomenon. Close examination of the technic of its elicitation makes it clear that it is based on the same stretching of the finger flexors as that in the finger flexor reflex, already described. The sudden, forcible, passive flexion of the end phalanx of the middle finger is followed by a sudden release, which consists of sudden stretching of the flexor muscle of the third finger with subsequent reflexive bending. The stretching of one flexor muscle mechancially involves the other flexors as well. The Hoffmann reflex represents thus only a special technic of elicitation of the previously discussed finger flexor reflex. It is of course easier to provoke a sudden stretching by application of a direct blow to the volar surface of the finger tips than by use of the method of Hoffmann. Therefore Hoffmann's technic of elicitation is cruder than the method previously described. Hence it often occurs that the finger flexor reflex is elicited by the method described here while it is not obtained by Hoffmann's method.

In numerous textbooks and articles Hoffmann's reflex has been designated as a pyramidal sign, "equally as valuable as a Babinski sign." Grinker [107] asserted, to cite one of the latest statements, that on elicitation of the Hoffmann reflex the resultant movement is a flexion of the terminal phalanx when a lesion of the pyramidal tract exists. Purves-Stewart [108] said: "In health, the patient's thumb remains motionless, but in disease of the pyramidal fibers of the upper limb the thumb makes a quick reflex movement of flexion and adduction." In my opinion, to Hoffmann's sign applies all that has been said of the finger flexor reflex, since the two are based on the same mechanism and are therefore identical. It is essential to stress that however valuable a pyramidal sign the Hoffmann reflex may be, it is not in itself pathologic; it indicates, if outspoken, only a state of increased muscular tonus, which may be pyramidal, but may also be purely functional, and therefore is diagnostically insignificant. The Hoffmann reflex is so obviously a muscle stretch reflex, as are the finger flexor reflex and all the so-called tendon reflexes, that it is hardly necessary to criticize the view of Keyser [102] who stated that ". . . the Hoffmann reflex belongs to the group of defense movements, in contradistinction to the tendon reflexes."

It is interesting to note that despite the countless declarations that the Hoffmann sign is

107. Grinker,[39] p. 260.

108. Purves-Stewart, J.: The Diagnosis of Nervous Diseases, ed. 8, Baltimore, William Wood & Company, 1937, p. 540.

indicative of a lesion of the pyramidal tract, one finds in the literature numerous, scattered critical comments and observations which cast doubt on the value of this sign as an indication of a pyramidal lesion. Dana [91] stated: "Its presence generally indicates a pyramidal tract lesion, but it is not very trustworthy." Echols [105] was cautious enough to declare that "Hoffmann's sign almost always indicates a disturbance of the pyramidal pathways." He said "almost" rightly, since he elicited an unexplained Hoffmann sign in 1.63 per cent of male university students. Pitfield [103] stated, with some resignation, that the Hoffmann sign ". . . is confusingly present in ephemeral and functional disorders. It is a sign of disease or of some dysfunction of the body." Keyser [102] found a positive Hoffmann sign ". . . also in some functional cases associated with 'lively, deep reflexes.'" Perelman [98] noted some exceptions to the rule that Hoffmann's sign is positive only in the presence of organic lesions—exceptions that in his opinion needed further investigation. An opinion regarding the nature of the Hoffmann reflex most in accord with that expressed in this paper was stated by Brain [109]: ". . . The Hoffmann is probably an index of muscular hypertonia rather than of a pyramidal lesion as such. . . . It may be elicitable in a nervous individual with no organic disease." The word "probably" should be omitted, and the term "muscular hypertonia" is not quite correct, since the degree of muscle tonus necessary for the appearance of the Hoffmann sign lies completely within normal limits.

In 1912 Trömner [110] described a finger reflex which carries his name. He called it the finger phenomenon. The patient keeps his fingers flexed, and the examiner taps with his own middle finger the volar surfaces of the tip of the middle or the index finger of the patient. A flexion of all the fingers, including the thumb, constitutes a positive reflex. Weisz [111] observed that in cases of organic disturbance the Trömner reflex is positive when the arms become spastic and increases with the increase in spasticity; however, it may be absent when the spasticity is severe and contracture develops. It is absent in cases of fresh pyramidal lesions—for instance, in cases of apoplexy. It is obvious that this response is a finger flexor reflex elicited by stretching of the flexors of the middle or the middle and the index finger. The appearance and the degree of strength of this reflex depend on the tonus of the muscles and on the amount of brisk stretching to which the muscles have been subjected. This reflex may be distinct with pyramidal lesions, but by no means appears with these alone. To the Trömner reflex applies what has already been said about the finger flexor reflex. It is misleading, even wrong, to speak of the Trömner reflex as a pyramidal sign. Trömner,[110] in 1912, said that his reflex was analogous to the Babinski sign and was as pathognomonic for the arm as the Babinski sign is for the leg. In 1913 Trömner [112] asserted that he found this reflex always, and only, in cases of spastic paralysis of the arm. But ten years later, in 1923, he [113] confessed that in eliciting his phenomenon, "one may see mild flexion of the fingers with neuropathic conditions as well, but that stronger reactions indicate a pyramidal lesion." This, in essence, is practically a renunciation of the idea that the Trömner reflex is pathognomonic of a pyramidal lesion. It is of course impossible to ascertain in a given case when the Trömner reflex should be regarded as due to a lesion of the pyramidal tract and when to a functional disturbance. No such distinction can be made, since the Trömner reflex, though often latent, is a normal reflex and when strongly positive is only a pathologic exaggeration of a basically normal reflex.

Yet, in the last edition of his classic textbook, Sahli [114] spoke of a "Trömner finger phenomenon associated with a pyramidal lesion." Böhme [115] stated in his monograph on reflexes: "The Trömner reflex is to be regarded as analogous to the Rossolimo toe reflex and speaks diagnostically for a lesion of the pyramidal tract." Pool [116] listed the Hoffmann and the Trömner sign as reflexes ". . . due to central pyramidal tract lesions." In the last edition of his textbook, Bing [117] listed the reflex of Trömner among the pathologic reflexes associated with the spastic syndrome.

According to the view expressed in this paper, the Trömner reflex represents nothing more

109. Brain, R.: Diseases of the Nervous System, ed. 2, London, Oxford University Press, 1940, p. 45.

110. Trömner, E.: Fingerbeugephänomen, Neurol. Centralbl. **31**:603, 1912.

111. Weisz, S.: Ueber Pyramidenzeichen am Arm, Nervenarzt **6**:179, 1933.

112. Trömner, E.: Ueber Sehnen-resp. Muskelreflexe und die Merkmale ihrer Schwächung und Steigerung, Berl. klin. Wchnschr. **50**:1712, 1913.

113. Trömner, E.: Zur Technik der Reflexprüfung, Klin. Wchnschr. **2**:1810, 1923.

114. Sahli, H.: Lehrbuch der klinischen Untersuchungsmethoden, ed. 7, Leipzig, Franz Deuticke, 1932, vol. 3, p. 225.

115. Böhme,[82] p. 973.

116. Pool, J. L.: Manual Reflex, Bull. Neurol. Inst. New York **6**:372, 1937.

117. Bing, R.: Lehrbuch der Nervenkrankheiten, ed. 6, Berlin, Urban & Schwarzenberg, 1940, p. 167.

than a method for bringing about sudden stretching of the finger flexors necessary for elicitation of the finger flexor reflex—and not the best method. The method described previously, that of placing the examiner's index and middle fingers across the four, slightly bent fingers of the patient and then tapping his own fingers briskly, abruptly and sharply, is by far more efficacious. It is all the more so when one combines this technic with the method of reenforcement by asking the patient to bend his fingers slightly. By using both these methods one can elicit the finger flexor reflex more easily than by any other method, and one sees this reflex so commonly that it cannot be regarded as pathologic. The finger Rossolimo sign, as this finger flexor reflex is often termed, is not a mysterious, "primitive" sign, as Voss [118] called it, that must be explained phylogenetically; it is an ordinary reflex, such as can be elicited from any other muscle of the human body, with the only distinction that it exists in more latent form than some other muscle stretch reflexes.

This concept is the same as that of Cooper,[119] who suggested that the Trömner reflex ". . . may be the response to stretching of the flexor muscles or their tendons when a state of abnormally increased muscle tonus or abnormally lowered resistance of the threshold of reflex excitability exists" and that ". . . it is a tendon reflex rather than purely a defense withdrawal effect." I should go a step further and say that "a state of abnormally increased muscle tonus" is by no means a prerequisite for the appearance of this reflex; it is elicited under completely normal conditions of muscle tonus. Böhme,[115] who in 1927 stated that the Trömner reflex indicates a lesion of the pyramidal tract, said in a review [120] published a year later that a weak Trömner reflex can be found in cases in which there is a functional increase of reflexes. I would put it this way: A strongly positive Trömner sign may, but need not, be a pyramidal sign.

In a recent monograph on the pyramidal signs of the upper extremity, Lange [121] stated: "The Hoffmann-Trömner reflex has in my opinion the same significance as the Babinski sign." There is not the slightest doubt that such a statement is untenable and can only lead to serious diagnostic mistakes.

In 1926 Sterling [122] recommended that the technic of Rossolimo be applied to the fingers, as well as to the toes. The examiner taps the volar surface of the patient's finger tips with a short, elastic blow with all his fingers. Flexion of all fingers follows. Sterling observed this reflex chiefly in cases of lesions of the pyramidal tract. Only in certain cases did he find it positive when there was no spastic paralysis of the corresponding extremity. In these cases the triceps and radial reflexes were exaggerated at the same time. This statement must be understood as an admission that this reflex, which is of course identical with the finger flexor reflex, is not in any way pathognomonic of a pyramidal lesion. Since a certain amount of tonus of the finger flexors is essential for the appearance of the finger Rossolimo sign, it is understandable that Johnsson,[123] on investigating the Sterling reflex in cases of early hemiplegia, found that it was absent in the first weeks, but appeared later.

Russetzki,[124] in commenting on Sterling's article, said that in 1925 he described in the Russian literature a phenomenon which exactly corresponded to Sterling's.

In 1935 Rosner [125] described a reflex which he called the "finger-thumb reflex." He, too, applied the method of Rossolimo to the fingers. Instead of tapping one or two fingers, as Trömner did, he tapped all four fingers, as Sterling did. He at first did not mention the work of Trömner or Sterling. Although he seriously attempted to emphasize the importance of his reflex as a pyramidal sign, he once mentioned that in normal persons, too, there may occur a slight bending movement of the second to the fifth finger, but he maintained that it is easy to distinguish this mild movement of the fingers from the real reflex movement. In my opinion the movements are identical; the difference is one only of degree. Although it is easy to distinguish the reflex finger flexion in a case of advanced spastic paralysis from that in normal persons, there is no way to differentiate slight

118. Voss, G.: Das Verhalten der spastischen Reflexe im Säuglings- und im frühen Kindesalter, Monatschr. f. Kinderh. **50**:331, 1931.

119. Cooper, M. J.: Mechanical Factors Governing the Trömner Reflex, Arch. Neurol. & Psychiat. **30**: 166 (July) 1933.

120. Böhme, A.: Methoden der Reflexprüfung beim Menschen, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1938, vol. 5, pt. B, p. 619.

121. Lange, O.: Sinais piramidais nos membros superiores, Rev. Assoc. paulista de med. **18**:351, 1941.

122. Sterling, W.: Les phénomènes des doigts analogues aux signes de Babinski et de Rossolimo, Rev. neurol. **2**:82, 1926.

123. Johnsson, V.: Examination of a Hand Reflex Described by Sterling, Hygiea **97**:401, 1935; abstracted, Zentralbl. f. d. ges. Neurol. u. Psychiat. **78**:37, 1935.

124. Russetzki, J.: Sur le phénomène des doigts analogue au signe de Rossolimo décrit par W. Sterling, Rev. neurol. **1**:317, 1927.

125. Rosner, R.: Ein Zeichen der Pyramidenbahnläsion an der oberen Extremität, Wien. klin. Wchnschr. **48**:800 and 1291, 1935.

differences in the degree of flexion—differences which are of practical diagnostic importance. Rosner [125] offered another sign by which his reflex may be proved pathologic and indicative of a lesion of the pyramidal tract. If, in addition to the four fingers, the thumb makes a movement of flexion, then, he claimed, the reflex is definitely pathologic and indicates a lesion of the pyramidal tract. This statement is not correct. On elicitation of the finger flexor reflex by the method described earlier, one often sees an associated flexion of the thumb in completely normal persons. This, then, can by no means be regarded as pathologic, as Rosner assumed. Rosner later strove to point out a distinction between his method of elicitation and that of Trömner. Such a distinction is of little significance. It really does not matter whether flexion is secured by the tapping of one finger or of two (Trömner) or of all four (Rosner). In his later article Rosner [126] was more cautious in evaluating his sign as pyramidal. He stated that the presence of this reflex may, "under certain circumstances," be considered as a pyramidal sign. Zajdorf,[127] a pupil of Bing, in a comparative study of the Trömner and the Rosner reflex, found the former more sensitive, but mentioned that both may be positive in the presence of functional disease of the central nervous system. Contradictory to this is his previous statement that "the finger flexion phenomenon is a pathologic reflex that appears with a lesion of the motor tract above the seventh and eighth cervical segments."

Since any muscle can be stretched, and its reflex thus elicited at any point along its entire course, from origin to insertion, it is understandable that the finger flexor reflex can be elicited not only from the finger tips but from proximal points as well. Von Bechterew,[128] as far back as 1902, mentioned the possibility of eliciting a reflex flexion of the fingers on mechanical irritation of the volar aspect of the forearm and the hand. He mentioned in particular the reflex flexion of the fingers, hand and forearm when the tendons of the flexors above the ligamentum carpi transversum were tapped. He stressed that these reflexes are not constant, that they are often seen in normal persons and may appear extremely exaggerated under pathologic conditions. Von Bechterew's pupil Nikitin [129] obtained reflexes from the flexors of the hand bilaterally in 62 per cent of normal persons. Goldscheider [130] described the same reflex as a flexion tendon reflex which is elicited by tapping the tendons at the ligamentum carpi transversum, the hand being dorsiflexed. He obtained the same effect, even more constantly, from the flexor muscles of the forearm. Goldscheider found this reflex in 45 per cent of normal persons and observed that it was exaggerated under pathologic conditions and in patients with neuroses. Bing [117] listed under normal "tendon and bone reflexes" a flexor tendon reflex produced by a tap on the flexor tendons at the wrist joint, resulting in finger flexion. Foerster [131] designated as a finger flexor reflex a response that can be elicited from the flexor tendons on the volar side of the forearm. This reflex, he stated, is normally weak and hardly elicitable. It is greatly exaggerated under spastic conditions of the arm and can then be elicited also by tapping of the lower end of the radius and the palm of the hand. I cite these examples only to show that it is possible to elicit a finger flexor reflex from any point over the entire length of the finger flexor muscles and their tendons. Such a reflex can be elicited in normal persons.

To elicit a deep muscle reflex it is not necessary to tap the muscle or its tendon directly, but it is sufficient to produce concussion of the underlying bone by tapping it.

In 1908 Jacobsohn [132] described a finger flexion reflex which consisted of flexion of the fingers on a mild tap of the lower end of the radius or in its neighborhood on the dorsal side of the forearm. He expressed the opinion that this reflex is analogous to the Babinski sign and a valuable sign in cases of spastic paralysis affecting the upper extremities. In 1910 Babinski [133] described the same phenomenon of flexion of the fingers when the lower end of the radius is tapped as when the "radioperiosteal reflex" is elicited. He saw in it a pyramidal sign, as did Bing [117] and Russetzki.[134] The latter even

126. Rosner, R.: Der Fingerreflex—als Pyramidenzeichen der oberen Extremität, Schweiz. med. Wchnschr. **70**:210, 1940.

127. Zajdorf, A.: Das Fingerbeugephänomen, Inaug. Dissert., Basel, 1937.

128. von Bechterew, V. M.: (*a*) On the Carpo-Phalangeal Reflex, Obozr. psikhiat., nevrol. **7**:487, 1902; (*b*) Ueber den Carpometacarpalreflex, Neurol. Centralbl. **22**:195, 1903.

129. Nikitin, M. P.: Ueber den Bechterew'schen Beugereflex der Zehen, Berl. klin. Wchnschr. **45**:1643, 1908.

130. Goldscheider, A.: Diagnostik der Krankheiten des Nervensystems, ed. 4, Berlin, Gustav Fischer, 1911, p. 50.

131. Foerster, O., in von Schjerning, O.: Handbuch der ärztlichen Erfahrugen im Weltkriege, Leipzig, Johann Ambrosius, Barth, 1922, vol. 4, p. 270.

132. Jacobsohn, L.: Ueber den Fingerbeugereflex, Deutsche med. Wchnschr. 1908, vol. 2, p. 1971.

133. Babinski, M.: Inversion du réflexe du radius, Bull. et mém. Soc. méd. d. hôp. de Paris **30**:185, 1910.

134. Russetzki, J.: Le syndrome pyramidal, Acta med. Scandinav. **73**:286, 1930.

expressed the opinion that the reflexes of Jacobsohn and von Bechterew are "grasping reflexes," which certainly they are not. To consider as pathologic a reflex finger flexion which follows tapping of the lower part of the radius is not correct; it is at variance with experience gathered since Jacobsohn's and Babinski's publications. Curschmann [101] found that the reflex described by Jacobsohn is not infrequent in patients with neuroses, especially young hysterical and neurasthenic persons. Sahli [135] stated, in referring to the Babinski modification of the von Bechterew–Jacobsohn reflex: "I must deny the diagnostic importance of this reflex, since I have observed it in exactly the same form in normal persons." Hoge,[136] who expressed the opinion that this reflex is pathologic, observed it in a few persons—neurotic patients—who showed no other signs or symptoms of organic nervous disease. "Again and again," stated Antoni,[137] "for instance in cases of neurasthenic hyperreflexivity, I see, on tapping the end of the radius, a simultaneous jerk of the flexors of the elbow and of the fingers." Foix and Chavany [138] noted that when one tapped the processus styloides radii, one "always" observed flexion of the fingers of mild degree, together with flexion of the forearm. Wilson,[139] too, evidently concluded that this finger flexion was normal, since he spoke of the "finger flexion part of the complete radial or supinator reflex." Pitres and Testut [140] "sometimes" observed this accompanying flexion of the fingers. It is statistically impossible to determine the frequency of finger flexion on tapping of the processus styloides radii, since much depends on the direction of the blow and the position of the forearm. There can be no doubt, however, that this reflex is in essence a normal one, though sometimes not distinctly perceptible; it appears more distinctly in cases of reflex hyperirritability, of functional or organic nature. In itself it by no means indicates a lesion of the pyramidal tract.

135. Sahli, H.: Lehrbuch der klinischen Untersuchungsmethoden, ed. 7, Leipzig, Franz Deuticke, 1932, vol. 3, p. 224.

136. Hoge, M. W.: The Radio-Phalangeal Reflex in Lesions of the Pyramidal Tract, Interstate J. Med. **19**:787, 1912.

137. Antoni, N.: Zur Kritik der irrtümlich sogenannten Sehnen- und Periostreflexe, Acta psychiat. et neurol. **7**:9, 1932.

138. Foix and Chavany, in Roger, G. H.; Widal, F., and Teissier, P. J.: Nouveau traité de médecine, Paris, Masson & Cie, 1928, vol. 18, p. 574.

139. Wilson, S. A. K.: Neurology, London, Edward Arnold & Co., 1940, vol. 2, p. 1309.

140. Pitres, A., and Testut, L.: Les nerfs en schémes, Paris, Gaston Doin, 1925, p. 687.

In 1926 Kempner,[141] unaware of any former publications, described this reflex and was reminded by Jacobsohn-Lask [142] that the phenomenon had been discovered by him eighteen years previously.

Since concussion of the bones of the forearm can produce the finger flexor reflex, it is worthy of note that this flexion of the fingers can be achieved by tapping not only the radius (Babinski, Jacobsohn, and Kempner) but the posteroinferior surface of the ulna (Purves-Stewart [143]). Von Bechterew [144] noted flexion of the fingers when the acromion or the coracoid process was tapped.

In 1902 von Bechterew [128a] reported in the Russian literature a "carpophalangeal reflex" as a joint reflex. In a poor translation of this article into German,[128b] this reflex is called the "carpometacarpal reflex," under which name it has been known since. Von Bechterew's original name is more appropriate. As I mentioned in the introduction, a muscle stretch reflex may be elicited not only by tapping the side of the extremity from which the muscle originates and into which it is inserted, but by tapping the opposite, or convex, side, the joint being thus depressed and the muscle indirectly stretched. It follows therefore that the stretching of the finger flexors may be achieved by tapping the dorsum of the hand. Indeed, the reflex of von Bechterew consists of flexion of the fingers when the dorsal surface of the carpal and the adjoining part of the metacarpal bones are tapped, especially laterally.

In his first article, von Bechterew expressed the opinion that this reflex indicated a lesion of the pyramidal tract. In a later article [145] he noted that the reflex appears in cases of increased reflex irritability. Galant [146] called it pathologic, and Jacobsohn [132] and Lewandowsky [147] found it associated only with organic lesions of the pyramidal tract. Galant [146] was able to elicit the reflex also by tapping the metacarpophalangeal and the interphalangeal joint lines. Since the reflex is nothing but a finger flexor reflex, it cannot be regarded as pathologic. In line with

141. Kempner: Ueber eine Art Mendelschen Reflexes an der Hand, Klin. Wchnschr. **5**:1255, 1926.

142. Jacobsohn-Lask, L., in discussion on Kempner,[141] p. 1471.

143. Purves-Stewart,[108] p. 536.

144. von Bechterew, V. M.: On the Acromion or Apical Reflex, Obozr. psikhiat., nevrol. **7**:181, 1902.

145. von Bechterew, V. M.: Ueber Reflexe distaler Abschnitte der oberen Extremität und über ihre diagnostische Bedeutung, Neurol. Centralbl. **24**:392, 1905.

146. Galant, S.: Die Reflexe der Hand, Ztschr. f. d. ges. Neurol. u. Psychiat. **43**:260, 1918.

147. Lewandowsky,[80] p. 605.

this concept are the observations of Goldstein,[148] who noted von Bechterew's carpometacarpal reflex in cases of purely functional nervous disorders, such as neuroses with increased general reflex irritability. Investigations in Sahli's[135] clinic proved that this reflex occurs also in normal persons. Bickel[149] emphasized that it may be elicited in cases in which there is only mild functional reflex hyperirritability. Beck[150] found that von Bechterew's carpometacarpal reflex was more or less distinct in normal persons when the hand was dorsiflexed at the wrist joint, i. e., when the flexors of the fingers were stretched. It is interesting that Beck found this reflex reversed, dorsiflexion of the fingers taking place when the dorsum of the hand was tapped if the hand was volar flexed.

Since von Bechterew's investigations, different methods have been described for elicitation of finger flexion by tapping parts of the dorsum of the hand: Sicard and Cantaloube[151] elicited a "reflex of the thumb, index, little finger and interosseous muscles"; Niculesco,[152] a "reflex of the interosseous muscles," a "metacarpothenar reflex" and a "metacarpohypothenar reflex," and Coppa,[153] a "reflex of the fifth metacarpal bone." The work of all these men proved only that one can effect stretching of a single finger flexor, and thus elicit reflex flexion of a single finger, from any point over the dorsum of the hand or of the metacarpal bones. It is of course easier to effect stretching of a finger flexor by direct tapping of the volar surface of the finger tips than by the indirect method, namely, tapping of the dorsum of the hand or the radius. Thus it is understandable that Sterling[122] found the finger Rossolimo sign twice as common as the reflex of Jacobsohn and that Johnsson[154] found it the most common of all signs and phenomena which supposedly indicate a pyramidal lesion. But all the aforementioned reflexes which are characterized by flexion of the fingers represent one and the same reflex, which reflex may be more easily elicited by one method than by another. The ease with which the finger Rossolimo sign can be elicited distinctly in the presence of the slightest pyramidal lesion is due simply to the fact that this reflex is basically normal and the most minute increase in tonus is sufficient to make it distinct.

The identity of the finger flexor reflex and other so-called tendon (i. e., muscle stretch) reflexes is shown also by the fact that with pyramidal lesions the finger flexors show a clonus of the same character as the quadriceps muscle (patellar clonus) and the muscles of the foot (ankle clonus). Noïca[155] pointed out the similarity of these three clonuses.

All the adjectives and proper names which have been used to designate this reflex of the finger flexors, and all those that may follow—since there is probability of further "rediscovery" and development of new technics of elicitation—belong in a book on the history of neurology. In any textbook of neurology belongs *one* name—the finger flexor reflex. In describing a case, Johnsson[154] stated: "The hand Rossolimo sign (Sterling's reflex) and the Trömner reflex were positive on the right side." Would it not be simpler, instead of using these three names, to say plainly: "The finger flexor reflex was positive"?

HAND FLEXOR REFLEX

Exactly as do the flexors of the fingers, so do the flexors of the hand react to brisk stretching with contraction. This constitutes the hand flexor reflex. The technic is identical. The two reflexes are often elicited at the same time. The tendons of the flexors of the hand may be tapped on the volar side of the forearm at the ligamentum carpi transversum or higher. The same reflex may be elicited by a tap on the dorsum of the hand or of the forearm while the hand is loosely supported at the palm by the examiner. Here the direction of the blow is important. This reflex is not constant, but certainly appears in normal persons and is greatly exaggerated in patients with pyramidal lesions, occasionally even to the state of hand clonus. This clonus appears only when other, and more striking, signs had appeared earlier; it is hardly necessary to give it a special name: The term the "hand phenomenon of Dejerine"[156] has sometimes been used. Of course the extensors of the hand react,

148. Goldstein, M.: Die Gelenkreflexe der Hand und ihre klinische Bedeutung, Ztschr. f. d. ges. Neurol. u. Psychiat. **61**:1, 1920.

149. Bickel, H.: Ueber die diagnostische Bedeutung der Knochenreflexe, Deutsche med. Wchnschr. **38**:2399, 1912.

150. Beck, E.: Reflexbiologische Studien, J. f. Psychol. u. Neurol. **29**:216, 1923.

151. Sicard, J. A., and Cantaloube, P.: Les réflexes musculaires du pied et de la main, Presse méd. **24**: 145, 1916.

152. Niculesco, I.: Le réflexe des interosseux, abstracted, Rev. neurol. **28**:384, 1921.

153. Coppa, E.: Contributo allo studio della reflettivita della mano in condizioni patologiche, Cervello **7**: 164, 1928.

154. Johnsson, V.: Case of Operated Tumor of Spinal Cord with Inversion of Radial Reflex and Facial Paralysis, Hygiea **96**:625, 1934; abstracted, Zentralbl. f. d. ges. Neurol. u. Psychiat. **75**:685, 1935.

155. Noïca: Phénomènes réflexes par distension tendineuse, Rev. neurol. **26**:196, 1919.

156. Dejerine, J.: Sémiologie des affections du système nerveux, Paris, Masson & Cie, 1926, p. 946.

too, on brisk stretching with contraction. Such a reflex has been described by von Bechterew [145] as the "hand reflex" (percussion of the dorsal part of the lower part of the ulna) and by Sandoz [157] as a pathologic reflex of the upper extremity (percussion of the lower part of the radius). Dagnini,[158] who described this phenomenon as a "reflex of hand extension," was in error when he stated that it had never been described before. In order to elicit these reflexes a certain position of the hand and the forearm is necessary. The percussion brings about the dorsal extension of the hand. These reflexes of the extensors of the hand are clinically insignificant.

FINGER-THUMB REFLEX (MAYER)

This reflex was described by Mayer [159] in 1916. He first called it the "finger-thumb reflex" and then the "metacarpophalangeal reflex." The first name is more appropriate. In exceptional cases it is necessary, in order to avoid confusion with other reflexes, to add the proper name. This reflex consists of opposition and adduction of the thumb combined with flexion at its metacarpophalangeal joint and extension at its interphalangeal joint on firm passive flexion of the third to the fifth finger—especially the fourth finger—at the proximal joints. This reflex is positive in normal persons and absent in patients with pyramidal lesions. Though it may be absent bilaterally in normal persons, its unilateral absence constitutes one of the most delicate of the pyramidal signs. Because it is not a muscle stretch reflex, this reflex properly does not belong here but should be included with the postural reflexes. It is essentially a part of the "negative support reaction." It is mentioned briefly here to emphasize a practical point, disregard of which may lead to erroneous diagnostic conclusions. Not only may this reflex be lost but it may be exaggerated, and this may occur with a lesion of the frontomotor region of the brain. This exaggeration may be the only striking localizing sign. In such a case it may be extremely difficult to say on which side the reflex must be regarded as normal and on which as exaggerated or diminished. It must be assumed that this reflex, the arc of which passes through the cortex of the motor area, is inhibited by the premotor area.

157. Sandoz, P.: Sur un réflexe pathologique des membres supérieurs, Rev. méd. de la Suisse Rom. **32**: 533, 1912.

158. Dagnini, G.: Réflexe d'extension de la main dans les lésions des voies pyramidales, Rev. neurol. **1**: 413, 1934.

159. Mayer, C.: Zur Kenntnis der Gelenkreflexe der oberen Gliedmassen, Neurol. Centralbl. **35**:11, 1916.

PRONATOR REFLEX

When the volar surface of the lower part of the radius is tapped so that a jerky supination is effected, and the pronators are stretched, these pronators (the pronator teres and pronator quadratus muscles) contract briskly. This constitutes the pronator reflex. This reflex has been described under a diversity of names, such as "ulnar reflex," "radial-pronator reflex," "ulnar-pronator reflex" and "cubitopronator reflex." Landau [160] distinguished (*a*) a radial pronation reflex, (*b*) an ulnar pronation reflex and (*c*) a superior radial pronation reflex. These variously named reflexes differ only in that they are elicited by tapping different points. In all of them, however, it is the contraction of the same pronator muscles which constitutes the reflex. Therefore this reflex, regardless of the point of its elicitation, should be called pronator reflex, as von Bechterew [145] did in 1905. This phenomenon is best elicited when the forearm is resting on its ulnar border, either vertically or pronated at a slight angle. The aim of the tap is to bring about a slight, brisk supination. Suppose the left arm is before the examiner in a position for elicitation of the pronator reflex. The forearm may be compared to a vertical column which must be tipped to the right. This can be achieved either by pushing the top of the column to the right or by pushing its base to the left. In either case the effect will be the same—the column will tip to the right. So with the forearm; when one taps the volar surface of the lower end of the radius or the dorsal surface of the styloid process of the ulna or the fourth and fifth metacarpal bones, the same effect, namely, supination and stretching of the pronators, follows. It is hardly necessary, therefore, to report that there was loss of the cubitopronator and radiopronator reflexes, as Guillain [10] did, or to distinguish a radio pronator reflex and an ulnopronator reflex, as Monrad-Krohn did.[161] There is but one reflex. There are other ways by which one may elicit the response, for instance, by tapping the elbow laterally from the medial epicondyle at the point of origin of the pronator teres muscle. Tapping the lower end of the radius or the ulna, however, is by far the better method. A subtle technic is essential here. The reflex hammer must swing loosely; the tap must be soft and so directed as to effect stretching of the pronators exclusively or predominantly. The position of the forearm is important.

160. Landau, E.: Neuropathologische Kriegserfahrungen, Cor.-Bl. f. schweiz. Aerzte **44**:33, 1919.

161. Monrad-Krohn, G. H.: The Clinical Examination of the Nervous System, ed. 7, New York, Paul B. Hoeber, Inc., 1938, p. 127.

If this position is changed, the direction of the blow altered or the force of the blow increased, stretching of other muscles will result—for instance, the biceps, the brachialis, the triceps, the flexors of the hand and fingers or the extensors of the hand. One elicits completely different reflexes and their combinations, in strict dependence on the position of the forearm and the direction of the stroke. This variation was pointed out by von Bechterew[145]; Bickel[149]; Marie, Bouttier and Bailey[162]; Poppi,[163] and Antoni.[137] On careful clinical observation it is easy for any one to see the mechanism by which remote muscles are influenced by a single tap, especially in examination of a patient with muscular hypertonia. Here the absolute and direct dependence of a reflex movement on the stretching of the respective muscles is self evident. The reflexes appear unmistakably as direct results of stretching of the muscles. One does not need to assume, as Foerster[164] did, that some of the reflexes described here may also be due to stimulation of the receptors of the bones. Foerster spoke of these reflexes as "bone phenomena," while Goldstein[148] called them "periosteal reflexes"; yet they are nothing else than muscle stretch reflexes.

The clinical importance of the pronator reflex is considerable, especially in the diagnosis of an early lesion of the pyramidal tract affecting the arm. With such a lesion an increase in the tonus of the pronator muscles and the tendency of the forearm to assume a position of pronation may constitute one of the initial signs (Gierlich[165]). In later stages this tendency to pronation may be pronounced; the hypertonia of the pronators may be so increased that on brisk, passive supination a clonus may be elicited. The increase of the pronator reflex goes hand in hand with tension in the pronator muscles. Thus a slight unilateral exaggeration of the pronator reflex may be one of the first signs of a pyramidal lesion affecting the arm. In doubtful cases it is advisable to combine the examination of the pronator reflex with a test for hypertonia of the pronator muscles: Holding, loosely, the forearm of the patient, the examiner, with brisk, jerky, passive movements, brings the arm into a position of supination.

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162. Marie, P.; Bouttier, H., and Bailey, P.: Les supino-réflexes du membre supérieur, Rev. neurol. **29**: 451, 1922.

163. Poppi, U.: Bemerkungen über den Ulno-Pronator-Reflex, Wien. med. Wchnschr. **77**:59, 1927.

164. Foerster,[65] vol. 5, p. 175.

165. Gierlich, N.: Ueber das Promationsphänomen der Hand als frühes Kennzeichen einer Läsion der Pyramidenbahn, Deutsche Ztschr. f. Nervenh. **84**:69, 1925.

A SIMPLE METHOD OF DETERMINING FREQUENCY SPECTRUMS IN THE ELECTROENCEPHALOGRAM

OBSERVATIONS ON EFFECTS OF PHYSIOLOGIC VARIATIONS IN DEXTROSE, OXYGEN, POSTURE AND ACID-BASE BALANCE ON THE NORMAL ELECTROENCEPHALOGRAM

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Although the gross configuration of the normal electroencephalogram remains remarkably constant in the same person from day to day, and even from year to year, there is nevertheless a significant physiologic zone of variation in frequency, voltage and regularity, which often cannot be appreciated by inspection alone. The fundamental elements controlling brain potentials have been defined by Dubner and Gerard[1]; they include the intrinsic metabolic activity of the individual cells, the cellular membrane charges and the composition of the surrounding fluid mediums. As recorded by the electroencephalograph, the brain waves represent the electrical activity of masses of cortical cells discharging in a synchronous fashion. The nature of this synchronizing factor has not yet been clarified, but it may involve a group of cells acting as pacemakers. Alterations in the determinants of cellular metabolism, in membrane charge or in the composition of the surrounding fluid mediums generally affect frequency and voltage first, while regularity, which is an index rather of the synchronizing activity of the theoretic pacemaker mechanism, is influenced by more pronounced changes in these factors. In addition, the pacemaker mechanism is influenced by higher neural factors concerned with levels of attention and consciousness, such as those involved in opening the eyes or in falling asleep. These factors usually lead to abrupt changes in frequency, and they were controlled in this study.

The effects of gross alterations in the sugar, carbon dioxide and oxygen contents of the blood have been known for many years. Less well recognized are the effects of changes in some of these factors within a more physiologic range. An analysis of the magnitude of such physiologic effects is of value in two respects: First, observations on the effects of noxious factors, such as alcohol, drugs, anoxia and changes in atmospheric pressure, may be subject to errors in interpretation if the range and role of the major physiologic variables have not been previously assayed. Second, delineation of the zone of response to physiologic variables in normal subjects furnishes a valuable guide to study of similar responses in persons with disease states. In this respect the concept of threshold may prove useful.

The first quantitative analysis of the cortical frequency spectrum during both physiologic and pathologic alterations in constituents of the blood was made by Gibbs, Williams and Gibbs,[2] using the Grass-Fourier transform method.[3] This method of analysis yields a continuous spectrum of the energy in all frequencies from 1 to 60 per second in a strip of record of thirty seconds' duration. This study revealed shifts in distribution of energy during both physiologic and pathologic ranges of the various constituents of the blood. In other studies of this nature it has been attempted only to quantitate the total amount of normal activity (i. e., the per cent time alpha) or the total amount of abnormal activity (i. e., the delta index), and hence such investigations have been of limited value in the demonstration of continuous change through physiologic and pathologic zones.

For the purposes of clinical investigation there is real need for a simple method of determining frequency spectrums. Unfortunately, the Grass method is not available to most investigators. Further, it gives a rather complex expression of the distribution of frequencies, the analysis

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1. Dubner, H., and Gerard, R. W.: Factors Controlling Brain Potentials in the Cat, J. Neurophysiol. **2**:142, 1939.

2. Gibbs, F. A.; Williams, D., and Gibbs, E. L.: Modification of the Cortical Frequency Spectrum by Changes in Carbon Dioxide, Blood Sugar, and Oxygen, J. Neurophysiol. **3**:49, 1940.

3. Grass, A. M., and Gibbs, F. A.: A Fourier Transform of the Electroencephalogram, J. Neurophysiol. **1**:521, 1938.

of which is no small problem in itself. Gibbs and his associates [2] stated:

> . . . One cannot say what part of the energy at a given frequency is derived from relatively pure sine waves, which would appear as discrete and countable waves of that frequency in the unanalyzed record, and what part is derived from non-sinusoidal slower frequencies, the faster components of which are quite properly recorded as higher frequencies.

The complete objectivity of the method has much in its favor; one wonders, on the other hand, to what extent the indiscriminate analysis of all base line swings and superimposed oscillations includes artefacts of noncortical origin. Arrangement of the apparatus so that a simultaneous ink record is obtained does much to eliminate this objection.

Another method used by many investigators from time to time since the electroencephalogram has been known is simply the measurement of the wavelengths of successive waves. This method is exceedingly tedious and difficult, and for this reason alone it has never achieved any great popularity.[4]

It is our purpose in this paper to report on a simple quantitative method of expression of frequency distribution which has proved useful in the analysis of both normal and abnormal electroencephalograms. With this method of study of the normal electroencephalogram data on the effects of (physiologic) variations in the sugar and oxygen contents of the blood and of changes in posture are presented. Observations on hyperventilation, not properly a normal physiologic experience, during variations in the level of the blood sugar and in posture are also included because hyperventilation is commonly used by electroencephalographers as a diagnostic procedure. The conditions determining the appearance of slow waves during hyperventilation are of obvious importance.

METHODS AND MATERIAL

Electroencephalographic Method.—The instrument used was the standard, push-pull, ink-writing apparatus, constructed by Mr. Albert Grass. Bipolar fronto-occipital tracings were taken in all instances. In these studies regional variations were not considered. The usual precautions against extraneous interference, electrical and other kinds, were employed.

Analysis of Frequency Spectrums.[5]—With the usual ruled paper (large divisions at one second intervals), the number of complete waves in each one second strip of record was counted. The count for a total of 300 one second intervals was made, and the distribution of frequencies per second was expressed as a percentage of the whole. A complete wave was one which returned at least two thirds of the way to the base line. A wave which crossed the line dividing adjacent one second intervals was counted in the interval containing more than half the wave. Small superimposed waves were not counted. In general, it was found advisable to make full use of the high frequency filter to damp the superimposed fast oscillations of very low voltage (some of which were of muscle origin) so that the basic sine waves would have sharper definition. Stretches of low voltage fast activity, which were present in varying degrees in all records, were designated as such, and no attempt was made to estimate the individual waves, which were often not countable. When a given interval contained both countable waves and low voltage fast activity, the type which occupied the greater portion of that interval was arbitrarily selected for purposes of designation.

Such an analysis yields a "spectrum" of frequencies ranging from 1 to 12 per second, together with some low voltage activity. It should be emphasized, however, that this is not a true spectrum of frequencies in that the percentages of one second intervals containing 8 waves, 9 waves, 10 waves, etc., rather than the percentages of 8 per second waves, 9 per second waves, 10 per second waves, etc., are given. In other words, the distribution of waves per second, rather than the distribution of individual wavelengths, is determined. The latter is a tedious process and involves measurement of the length of each wave with a caliper of some sort. Our method may give a slightly false impression of the distribution of wavelengths greater and less than the dominant one, for waves of these frequencies will tend to be averaged with waves of the dominant frequency and hence may appear in somewhat lower proportion than is actually the case. For example, if 2 or 3 waves of 5 per second frequency should appear with 8 per second waves in a one second interval, the number of waves in that interval would be recorded as 6 or 7, and the figure would not reveal the presence of 5 per second waves. This will not obscure any shift toward faster or slower frequencies, and no error in interpretation will result if it is remembered that the method gives the distribution of average frequencies per second rather than the distribution of wavelengths. For practical purposes the method has proved thoroughly satisfactory in establishment of the magnitude of shifts in frequency under conditions in which such changes have been diffuse rather than paroxysmal. When the changes are paroxysmal (i. e., in epileptic records), a much longer strip must be analyzed before an accurate spectrum can be obtained.

Figure 1 illustrates the actual count of a sample record. Obviously, the more regular the record, the easier and more accurate is the analysis. Also, records with less than 50 per cent of low voltage fast activity are more satisfactory for determination of shifts within the range of countable frequencies, unless much longer strips are used. With increasing abnormality there is usually a corresponding increase in irregularity, but the resulting increased difficulty in counting is not a

4. Since this paper has been written, a new method of analysis of electroencephalograms, devised by W. Gray Walter (Appendix on a New Method of Electro-Encephalographic Analysis, J. Ment. Sc. **89**:222, 1943), has come to our attention. The equipment consists of a series of tuned reeds, covering the stretch from 1 to 20 cycles per second, which are energized by the output from the electroencephalograph. The apparatus is ingeniously arranged so that each ten second strip of record has traced over it a histogram of its spectrum. Gray stated that the analyzer shows a clear distribution of energy responding to physiologic stimuli, but no data are presented in this preliminary report.

5. One of us (G. L. E.) is primarily responsible for developing this method.

serious drawback, for the irregular waves are usually abnormally slow and hence yield a spectrum easily distinguished from normal. The practicability of the method for the study of changes in diffusely abnormal records has been demonstrated in another report on the reversible electroencephalographic changes associated with delirium.[6] In comparison of successive records it is sometimes helpful to plot the spectrums. Figure 2 illustrates typical spectrums.

With very regular records it was found sufficient to count a two hundred record strip. In these studies three hundred second strips were counted, except on the records taken during hyperventilation, which were three minutes (one hundred and eighty seconds) in length. An experienced person can count a three hundred second strip in ten minutes.

Methods of Chemical Analysis.—The dextrose content of the blood was determined by the Folin-Wu colorimetric method. The carbon dioxide and oxygen contents of arterial blood were measured by the Van Slyke manometric technic. The p_H of arterial blood was determined by means of the Leeds and Northrup potentiometer and glass electrode, the phosphate buffer of the Bureau of Standards being used as reference. Partial pressures of carbon dioxide and base bicarbonate concentrations were determined from Shock and Hasting's nomogram.

Material.—Twelve healthy men, medical students and physicians, ranging in age from 23 to 56 years, volunteered as subjects for these studies.

CHANGES IN DEXTROSE CONTENT OF THE BLOOD

The effects on the normal electroencephalogram of hypoglycemia of clinical magnitude are well known and need no further discussion. Gibbs and associates,[2] using the Grass analyzer, demonstrated an increase in energy in the slow frequencies as the blood sugar fell from 105 to 74 mg. per hundred cubic centimeters, while with a rise in the sugar content of the blood from 202 to 480 mg. per hundred cubic centimeters there was a slight shift to the fast side of the spectrum. Davis,[7] in a study of 40 healthy college students, found that as the blood sugar fell to a minimum of 53 to 83 mg. per hundred cubic centimeters the normal alpha activity of the electroencephalogram was increasingly replaced by slower waves, chiefly in the 6 to 8 per second range. No correlation between the magnitude of the shift and the levels of the blood sugar was attempted.

Method.—Eleven subjects were studied. Ten received an intravenous infusion of 0.5 Gm. of dextrose per kilogram of body weight as a 10 per cent solution of dextrose in distilled water, administered over a period of thirty minutes. Sugar levels were determined for blood from a vein in the arm, and electroencephalographic tracings were taken in the fasting, preinfusion state, at the end of the infusion and one, two and two and one-half hours after infusion. All examinations were made with the patient in the recumbent position. One subject was studied after a high carbohydrate breakfast and again eleven hours later, when the level of the blood sugar was much lower.

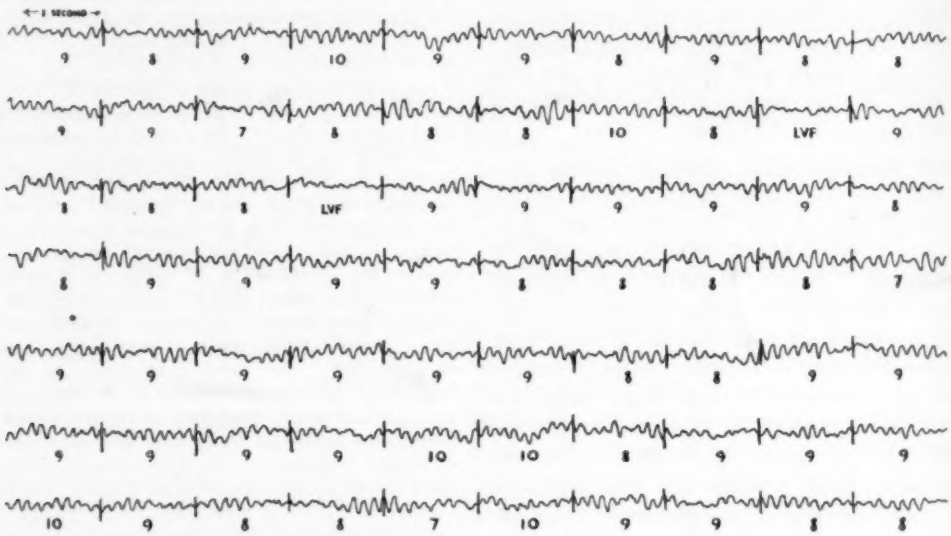

Fig. 1.—A sample electroencephalogram, illustrating the technic of counting waves.

Results.—Electroencephalograms may be divided into two types: records with more and records with less than 70 per cent alpha (8 to 12 per second) activity. As has been pointed out by other observers, the presence of high or of low alpha activity is a constant characteristic

6. Romano, J., and Engel, G. L.: Studies of Delirium: I. Electroencephalographic Data, to be published. Engel, G. L., and Romano, J.: Studies of Delirium: II. Reversibility of the Electroencephalogram with Experimental Procedure, Arch. Neurol. & Psychiat., to be published.

7. Davis, P. A.: Effect on the Electroencephalogram of Changing Blood Sugar Level, Arch. Neurol. & Psychiat. **49**:186 (Feb.) 1943.

of the individual record. Five records showed high alpha activity; 5 records, low alpha activity, and 1 record, well developed alpha activity from the right cortex and poor alpha activity, with many low voltage fast waves and some irregular slow rhythm from the left cortex. This subject had had speech difficulties (stammering and stuttering) as a child, but at the time of study he revealed no neurologic abnormalities.

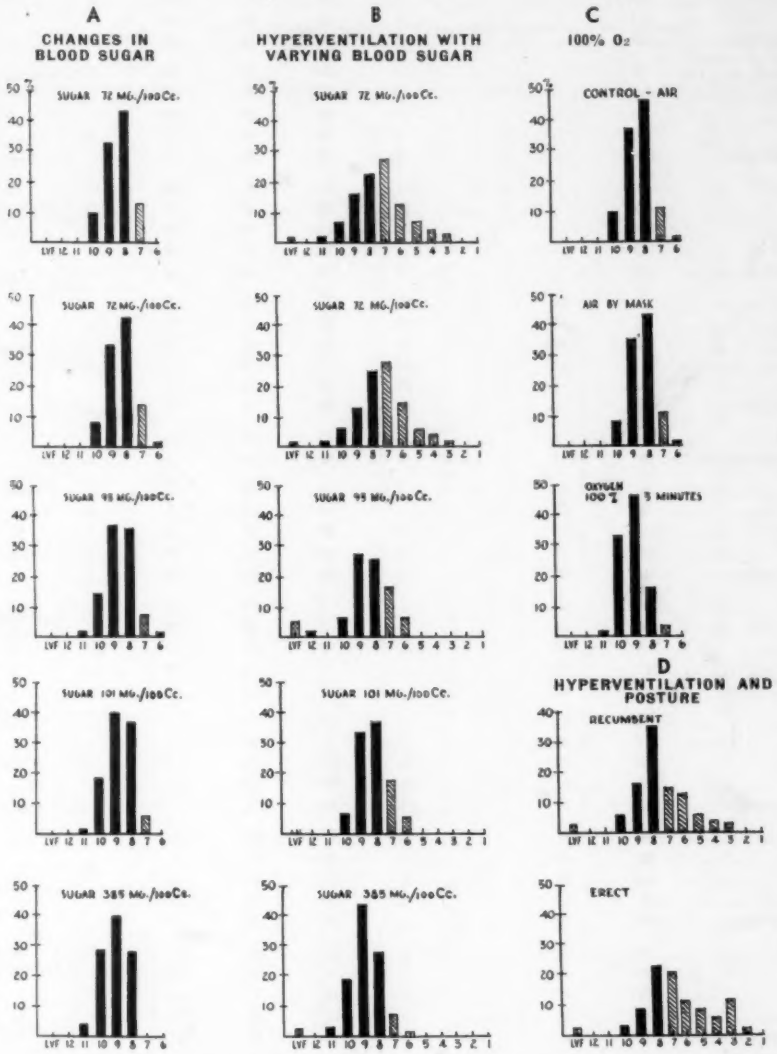

Fig. 2.—Spectrums showing the effects of variations in blood sugar (*A*), of hyperventilation and variations in blood sugar (*B*), of inhalation of oxygen and compressed air (*C*) and of hyperventilation and posture (*D*) in a single subject.

Examination of table 1 reveals that in the records with dominant alpha rhythm (nos. 1 to 6) there was a shift toward faster frequencies with higher levels of the blood sugar and toward slower frequencies with lower levels of the blood sugar. There were no levels of the blood sugar under 70 mg. per hundred cubic centimeters, and no subject experienced any symptoms suggestive of hypoglycemia. When 6 to 7 per second activity was present in the fasting state, it disappeared when the blood sugar became higher and, conversely, it increased in amount as the blood sugar fell below the fasting levels. The first column (*A*) in figure 2 illustrates the frequency spectrums of one subject during an intravenous dextrose tolerance test.

In the records with poor alpha rhythm no consistent trends in the frequency spectrums were observed. It is believed that this was due, at least in part, to the difficulty in counting these more irregular records and to the fact that an insufficient sample of countable frequencies was available in the three hundred second stretch.

TABLE 1.—*Effect of Level of Dextrose in the Blood on Frequency Spectrums in the Electroencephalogram* *

Subject	Status †	Blood Sugar, Mg. per 100 Cc.	Electroencephalographic Frequency Spectrums, Percentages								Alpha Activity (8-12/Sec.)
			LFV ‡	12/Sec.	11/Sec.	10/Sec.	9/Sec.	8/Sec.	7/Sec.	6/Sec.	5/Sec.	
E. B. F.	2½ hr.	72	..	..	..	10	33	43	13	..	..	86
Age: 37	2 hr.	..	..	..	..	8	34	43	14	1	..	85
	Fasting.	95	..	..	1	15	37	36	8	1	..	90
	1 hr.	101	..	..	1	18	40	36	5	..	..	95
	End of infusion.	285	..	..	3	29	40	28	..	..	..	100
G. E.	2 hr.	72	..	..	..	21	55	23	1	..	..	90
Age: 28	2½ hr.	76	..	..	..	26	55	18	1	..	..	99
	Fasting.	86	..	..	..	26	63	10	..	..	..	100
	1 hr.	120	..	..	1	34	48	16	1	..	..	99
	End of infusion.	290	..	..	1	33	61	5	..	..	..	100
J. R.	2½ hr.	76	..	..	..	11	41	35	11	2	..	87
Age: 34	2 hr.	79	2	..	..	13	40	36	9	..	..	89
	Fasting.	100	..	..	1	10	64	22	3	..	..	97
	1 hr.	122	..	..	..	16	58	23	1	..	..	97
	End of infusion.	342	..	..	2	24	50	15	..	..	..	100
L. S.	3 hr.	81	19	2	15	37	23	3	..	..	..	81
Age: 32	2½ hr.	85	16	..	14	46	17	7	..	..	..	84
	2 hr.	109	12	..	26	43	17	2	..	..	..	88
	Fasting.	127	15	2	14	47	19	2	..	..	..	85
	1 hr.	195	8	2	22	46	15	7	..	..	..	92
	End of infusion.	303	13	14	40	28	4	1	..	..	..	87
G. G.	8 hr. fast.	99	5	..	6	35	36	15	3	..	..	95
Age: 45	After dextrose, orally	180	1	1	11	49	31	7	..	..	..	99
J. McM.	2½ hr.	83	21	..	1	13	30	23	10	2	..	67
Age: 26	2 hr.	90	23	..	..	12	27	28	9	1	..	67
right	1 hr.	103	18	..	2	38	27	13	2	..	..	80
cortex	Fasting.	107	24	..	2	20	25	26	3	1	..	73
	End of infusion.	240	14	..	3	46	26	10	1	..	..	85
Left	2½ hr.	83	55	..	..	5	6	14	13	7	..	25
cortex	2 hr.	90	44	..	..	1	10	20	16	9	..	31
	1 hr.	103	60	..	..	2	12	12	10	4	..	26
	Fasting.	107	52	..	..	2	6	16	16	7	..	24
	End of infusion.	240	63	..	..	2	9	13	12	1	..	24
M. B.	2½ hr.	84	64	5	16	10	5	..	..	..	..	36
Age: 57	Fasting.	91	53	..	7	18	17	5	..	..	..	47
	2 hr.	93	32	3	23	33	8	1	..	..	..	68
	1 hr.	107	42	2	10	32	13	1	..	..	..	58
	End of infusion.	215	67	1	16	11	5	..	..	..	..	33
J. W.	2 hr.	70	47	2	6	13	22	10	..	..	..	53
Age: 29	2½ hr.	83	50	..	1	16	21	11	1	..	..	49
	Fasting.	95	45	2	8	20	21	4	..	..	..	55
	1 hr.	108	47	..	4	16	21	12	..	..	..	53
	End of infusion.	265	43	..	4	20	16	16	..	..	..	57
H. R.	1 hr.	70	39	..	1	12	21	23	3	1	..	57
Age: 29	2 hr.	76	39	..	..	7	19	25	8	2	..	51
	2½ hr.	82	47	..	1	19	10	24	5	..	..	49
	Fasting.	98	26	..	8	21	25	12	5	2	..	66
	End of infusion.	163	41	1	2	15	18	18	6	..	..	54
R. K.	1 hr.	71	76	..	2	2	8	8	..	..	..	20
Age. 42	2 hr.	87	84	..	..	3	9	4	..	..	..	16
	2½ hr.	88	86	..	1	2	3	8	..	..	..	14
	Fasting.	92	88	..	1	3	3	5	..	..	..	12
	After infusion.	157	82	..	1	5	8	4	..	..	..	18
R. McM.	2½ hr.	76	92	2	2	2	2	..	..	..	..	8
Age: 25	2 hr.	82	88	1	2	2	2	4	1	..	..	7
	Fasting.	95	90	1	4	3	1	1	..	..	..	10
	1 hr.	131	90	5	2	3	..	..	..	..	..	10
	End of infusion.	280	79	3	11	5	2	..	..	..	..	21

* Values are listed in order of increasing blood sugar levels.

† In this column, the number of hours indicates the period after the end of infusion.

‡ In this table, and in the following tables, LVF means low voltage fast activity.

It is also obvious from the data that the amount of alpha activity (and, conversely, the amount of low voltage fast activity) was independent of the level of the blood sugar.

Comment.—The magnitude of the changes observed is relatively small and is not likely to of dextrose as the major substrate for cerebral metabolism. The electrical frequency spectrum of the cortex apparently responds to changes in levels of the blood sugar within the normal and the hyperglycemic range, as well as in the hypoglycemic range, and in this respect the observa-

TABLE 2.—*Effect of Inhalation of 100 Per Cent Oxygen on Frequency Spectrums in the Electroencephalogram*

Subject	Experimental Procedure	Electroencephalographic Frequency Spectrums, Percentage: LVF	12/Sec.	11/Sec.	10/Sec.	9/Sec.	8/Sec.	7/Sec.	6/Sec.	Alpha Activity (8-12/Sec.)	Blood Sugar, Mg. per 100 Cc.	Comment
G. E. Age: 29	Before	..	..	..	25	51	24	..	..	100	...	
	Air by mask	..	..	..	27	47	24	..	..	100	...	
	100% oxygen	..	..	..	30	56	13	..	..	...	...	
	Before	1	..	..	21	44	29	5	..	94	110	
	100% oxygen, 5 min.	..	..	..	35	53	12	..	..	100	110	
	100% oxygen, 7 hr.	..	..	..	36	51	13	..	..	100	100	Continuous inhalation of oxygen, 7 hr.
	Before	2	..	2	31	48	16	2	..	94	85	
	100% oxygen, 5 min.	1	..	..	38	50	11	..	..	99	85	
E. B. F. Age: 37	Before	..	..	..	10	38	48	11	1	88	...	
	Air by mask	..	..	..	9	36	43	11	1	88	...	
	100% oxygen, 5 min.	..	..	1	32	47	17	3	..	97	...	
	After 5 min.	..	..	..	10	44	37	9	..	91	...	
	Before	..	..	..	8	35	42	13	3	85	123	
	100% oxygen, 5 min.	2	..	..	7	43	38	9	1	88	123	
	Before	1	..	..	6	37	39	16	1	82	115	
	100% oxygen, 5 min.	..	..	1	21	49	24	6	..	94	115	
	100% oxygen, 7 hr.	..	..	..	16	48	29	7	..	94	96	Continuous inhalation of oxygen, 7 hr.
	Before	..	..	..	10	47	37	6	..	94	109	
	100% oxygen, 8 min.	..	..	1	31	45	21	2	..	98	109	
G. G. Age: 45	Before	1	1	11	49	31	7	..	..	99	180	
	100% oxygen, 10 min.	1	..	13	47	24	5	..	..	99	180	
	100% oxygen, 8 hr.	..	2	14	45	30	9	..	..	100	113	Continuous inhalation of oxygen, 8 hr.
J. R. Age: 35	Before	..	..	..	13	52	34	1	..	99	...	
	Air by mask	..	..	..	12	53	31	4	..	96	...	
	100% oxygen, 5 min.	..	..	..	19	59	20	2	..	98	...	
	Before	..	..	..	20	52	25	3	..	97	96	
	100% oxygen, 5 min.	..	..	..	35	48	17	..	..	100	96	
	Before	..	..	..	14	61	23	2	..	98	87	
	100% oxygen, 5 min.	..	..	..	32	55	12	1	..	99	99	Inhalation of oxygen started 40 min. after control
	100% oxygen, 8 hr.	..	..	..	29	53	17	1	..	99	99	Continuous inhalation of oxygen, 8 hr.
H. R. Age: 29	Before	54	..	5	12	15	6	1	..	35	84	
	100% oxygen, 5 min.	44	1	11	18	11	5	..	..	46	84	
	100% oxygen, 8 hr.	28	1	16	21	18	13	3	..	69	97	Continuous inhalation of oxygen, 8 hr.
M. B. Age: 56	Before	32	6	20	25	15	2	..	..	68	72	
	100% oxygen, 5 min.	24	10	27	22	15	2	..	..	76	72	
F. B. Age: 30	Before	72	3	4	14	6	1	..	..	28	109	
	100% oxygen, 5 min.	79	5	11	3	2	..	..	..	21	109	
	100% oxygen, 8 hr.	78	5	10	5	2	..	..	..	22	111	Continuous inhalation of oxygen, 8 hr.

introduce any error in routine examination. However, in any studies of frequency spectrums during exposure to such factors as drugs, toxic substances and altered environmental conditions, particularly at threshold zones, it is apparent that changes in blood sugar during the course of the experiment must be controlled.

The mechanism of the effect of dextrose is not obvious but is possibly related to the role tions of Gibbs and his co-workers [2] are confirmed.

EFFECT OF INHALATION OF 100 PER CENT OXYGEN

The effects of low oxygen tensions have been described by other investigators and need not be discussed here. It is of some theoretic interest to know whether supernormal oxygen tensions

have any effect on the cortical frequency spectrums. Studies in which inhalation of 100 per cent oxygen is necessary during control periods (for example, high altitude exposure) make this of some practical interest. Gibbs and associates,[5] using rabbits, found no change in cortical frequency spectrums until the oxygen pressure was raised to 35 pounds (15.9 Kg.) of pure oxygen, and then there tended to be an increase in faster frequencies.

Method.—Seven subjects were studied in a total of 14 experiments. Electroencephalograms were obtained before, during and sometimes after the administration of 100 per cent oxygen by means of a Bulbulian type 14 demand mask modified for constant flow. Oxygen was supplied in excessive amounts, sufficient to keep the reservoir bag well distended at the height of inspiration. As an additional control, air, supplied from a tank of compressed air, was used instead of oxygen in 3 experiments. The duration of most experiments was only fifteen to twenty minutes, not long enough for any significant change in the level of the blood sugar. Six subjects were exposed to an atmosphere of 100 per cent oxygen for a total of seven to eight hours.

Results.—Inhalation of 100 per cent oxygen results in a slight, but significant, shift toward faster rhythms in the cortical frequency spectrums. This was most obvious in the records with regular, dominant alpha activity, but a trend was also present in the records with poor alpha activity. This effect was observed both during short (five to ten minute) and during long (seven to eight hour) exposures, although with the longer period the changes were less obvious in 3 instances, owing to a fall in blood sugar during that period. When, as an additional control, compressed air was substituted for 100 per cent oxygen, there was no effect on the frequency spectrums. The close similarity between the frequency spectrums obtained at the start of the experiment and those obtained during the inhalation of air through the mask provides an incidental check on the accuracy of the analytic method in the regular, dominant alpha records (fig. 2 *C*).

TABLE 3.—*Effect of Changes in Posture on Frequency Spectrums in the Electroencephalogram*

			Electroencephalographic Frequency Spectrums, Percentage									
Subject	Position of Subject	Blood Pressure	LVF	12/Sec.	11/Sec.	10/Sec.	9/Sec.	8/Sec.	7/Sec.	6/Sec.	Alpha Activity (8-12/Sec.)	Blood Sugar, Mg. per 100 Cc.
G. E.	Recumbent.....	114/ 64	3	..	..	30	52	14	..	..	97	104
Age: 28	Erect, 15 min.....	120/ 70	5	..	2	32	45	15	..	..	..	104
	Recumbent.....	104/ 70	5	..	..	19	47	25	4	..	91	91
	Erect, 17 min	108/ 80	3	..	2	22	43	28	3	..	94	91
	Recumbent.....	106/ 66	..	..	1	31	47	20	1	..	99	103
	Erect, 8 min.....	112/ 78	2	..	3	33	37	23	2	..	96	103
E. B. F.	Recumbent.....	115/ 80	..	..	2	12	34	42	10	..	90	100
Age: 37	Erect, 17 min.....	126/100	..	..	2	11	35	42	9	1	90	100
	Recumbent.....	108/ 80	9	..	..	10	31	40	8	2	81	96
	Erect, 5 min.....	116/ 94	..	..	..	9	27	49	19	..	85	96
	Recumbent.....	108/ 88	3	..	1	15	34	36	10	1	86	95
	Erect, 12 min.....	118/ 94	1	..	..	7	46	36	9	1	89	95
J. R.	Recumbent.....	120/ 85	5	..	1	16	59	18	1	..	94	87
Age: 33	Erect, 14 min.....	108/ 70	4	..	..	15	65	14	1	..	94	87
L. S.	Recumbent.....	120/ 82	15	6	35	33	10	1	..	..	85	..
Age: 32	Erect, 13 min.....	134/ 98	14	2	46	35	3	..	..	..	..	..
M. A. B.	Recumbent.....	126/ 80	40	8	20	23	8	1	..	..	60	81
Age: 57	Erect, 14 min.....	122/ 85	45	5	17	23	9	1	..	..	55	81
R. McM.	Recumbent.....	130/ 90	89	2	3	2	4	..	..	..	11	77
Age: 25	Erect, 10 min.....	118/ 92	91	3	2	1	3	..	..	..	9	77
H. W. R.	Recumbent.....	106/ 56	68	1	4	12	7	5	3	..	29	..
Age: 29	Erect, 20 min.....	108/ 75	68	3	1	7	11	7	3	..	29	..

Comment.—No studies of the gas content of arterial blood were carried out on these subjects. However, from other observations it is known that the inhalation of 100 per cent oxygen raises the oxygen saturation of arterial blood to 100 or 105 per cent, the supernormal figure being due to saturation of the plasma with oxygen. It cannot be established from these observations whether the effects noted are due to the increased oxygen tension itself or to changes in the carbon dioxide tension around the cortical cells, since the ability of the capillary blood to take up carbon dioxide is somewhat diminished in the presence of higher oxygen saturation of arterial blood. Whatever the mechanism, these data

again illustrate the readiness with which the electrical activity of the brain responds to alterations in environment of physiologic magnitude.

EFFECTS OF CHANGES IN POSTURE

Seven subjects were studied in 11 observations on the tilt table. There was no difference in the cortical frequency spectrum when the subject was in the erect position and when he was recumbent as long as the blood pressure remained essentially unchanged. The changes associated with orthostatic hypotension are described elsewhere.[8] The absence of any effect of change in posture on the resting electroencephalogram was expected and contrasted with the pronounced effect of changes in posture during hyperventilation.

The data present in table 3 give further evidence of the reproducibility of frequency spectrums in the same person at similar levels of the blood sugar.

HYPERVENTILATION

Hyperventilation is routinely used by most electroencephalographers as a diagnostic aid, but there is considerable disagreement as to the limits of the normal reaction. Only the appearance of the wave and spike pattern is regarded as abnormal by some observers, while others consider as abnormal any appreciable amount of high voltage slow waves of a frequency less than 5 per second. Further, in clinical studies at least, it is impossible to standardize intensity, and sometimes even duration, of hyperventilation because of difficulty in cooperation. An assay of the magnitude of response to ordinary physiologic variables is thus of considerable importance in establishment of criteria of normality.

Blood Sugar.—Variations in the level of blood sugar have been found to influence significantly the appearance of slow waves during hyperventilation.[9] The results of quantitative studies of the magnitude of this effect through a wide range of blood sugar levels and its correlation with changes in acid-base balance in arterial blood are not yet available. Nine of the subjects for whom data are listed in table 1 were studied during the dextrose tolerance tests, the technic of which has already been described. In table 1 are indicated the prehyperventilation frequency spectrums for each level of the blood sugar. The data for hyperventilation are present in table 4. All examinations were carried out with the subject in the recumbent position. Blood was taken from the femoral artery just before hyperventilation and, again, during the last minute of hyperventilation. Withdrawal of the samples usually took about thirty seconds. For the second sample the electroencephalograph operator signaled at the appearance of sustained large slow waves, or at the end of one hundred and fifty seconds if no large slow waves had appeared by that time. The samples of arterial blood were analyzed for the oxygen content, the carbon dioxide content and the p_H. From 3 subjects samples were obtained in the fasting state and two and a half hours after the infusion; from 6 subjects the first sample was drawn at the end of the infusion and the second two and a half hours later. All subjects hyperventilated as vigorously as possible for one hundred and eighty seconds, but in many instances there were unavoidable variations, usually due to alteration in awareness during the height of the reaction.

The results, presented in table 4, may be summarized as follows:

1. The amount of slowing in the electroencephalogram on hyperventilation tended to vary inversely with the level of the blood sugar after the infusion of dextrose (fig. 2 *B*). The blood sugar was not the sole determining factor, however, for when the results were listed in order of increasing blood sugar levels, the response during the fasting state was found to be slightly inconsistent in 7 instances (less slowing in 5 and more slowing in 2) as compared with the frequencies at similar levels of the blood sugar in the postinfusion state. This series is too small to establish whether these inconsistencies were due to variations in respiratory exchange during hyperventilation at different times or whether the fasting state differed in some other respect from the postinfusion state at comparable levels of the blood sugar.

2. The intravenous infusion of dextrose in itself did not appear to influence the magnitude of the change in acid-base balance resulting from hyperventilation.

3. With high levels of the blood sugar even maximal shifts in the acid-base balance of arterial blood resulted in only minor changes in distribution of frequencies. Conversely, with low levels of the blood sugar a much smaller shift in the acid-base balance sufficed to bring out significant slowing.

8. Engel, G. L.; Romano, J., and McLin, T. R.: Vasodepressor and Carotid Sinus Syncope: Clinical, Electroencephalographic and Electrocardiographic Observations, Arch. Int. Med., to be published.

9. Engel, G. L., and Margolin, S.: Clinical Correlation of the Electroencephalogram with Carbohydrate Metabolism, Arch. Neurol. & Psychiat. **45**:890 (May) 1941. Davis, H., and Wallace, W.: Factors Affecting Changes Produced in the Electroencephalogram by Standardized Hyperventilation, ibid. **47**:606 (April) 1942.

TABLE 4.—*Effect of Hyperventilation at Varying Levels of the Blood Sugar on Frequency Spectrums in the Electroencephalogram* *

Subject	Time After Infusion	Status †	Period of Hyperventilation Preceding Arterial Puncture, Min.	Arterial Blood: Carbon Dioxide Content, Vol. %	Arterial Blood: Carbon Dioxide-Combining Power, Mm. Hg ($BHCO_3$)‡	Arterial Blood: p_H	Arterial Blood: Oxygen Tension, Vol. %	Blood Sugar, Mg. per 100 Cc.	Electroencephalographic Frequency Spectrum (180 Sec. of Hyperventilation), Percentage: LVF	12/Sec.	11/Sec.	10/Sec.	9/Sec.	8/Sec.	7/Sec.	6/Sec.	5/Sec.	4/Sec.	3/Sec.	2/Sec.	1/Sec.	Alpha Activity (8-12/Sec.)
E. B. F. Age: 37	2½ hr.	Resting	170	42.9	38	23.5	7.41‖	19.3	72	1	..	1	7	17	22	27	13	7	3	2	..	..	47
		HV		33.0	13 ?	19.7 ?	7.8 ?	20.6														
	2 hr.	HV	...	....	....	....	....	....	72	1	..	1	6	13	25	28*	15	7	3	1	..	..	45
	Fasting	Resting	200	43.4	38	24	7.42	19.0	95	5	1	..	6	28	26	17	6	..	..	..	..	..	72
		HV		32.2	17	18.8	7.66	20.1														
	1 hr.	HV	...	....	....	....	....	....	101	1	..	..	7	33	36	18	5	..	..	..	..	..	76
	End of infusion	HV	...	....	....	....	....	....	385	2	..	2	19	43	27	7	1	..	..	..	..	..	91
G. E. Age: 28	2 hr.	HV	...	....	....	....	....	....	72	..	..	..	5	17	17	15	13	10	7	11	5	..	39
	2½ hr.	Resting	120	47.7	41	25.5	7.41	18.0	76	..	..	..	4	16	17	10	10	7	10	17	8	..	37
		HV		35.5	16.5	20.5	7.71	18.6														
	Fasting	Resting	120	44.1	37	24.0	7.43	18.2	86	..	..	..	9	32	40	14	5	1	..	..	..	..	81
		HV		37.2	21.5	21.0	7.60	18.6														
	1 hr.	HV	...	....	....	....	....	....	120	..	..	..	10	44	31	13	2	..	..	..	..	..	85
	End of infusion	HV	...	....	....	....	....	....	...	..	..	2	13	47	31	6	..	..	..	..	..	..	94
J. R. Age: 34	2½ hr.	Resting	160	46.4	42	25	7.39	18.7	76	..	..	..	2	6	16	16	27	18	8	6	..	..	24
		HV		34.7	16	19.3	7.69	19.8														
	2 hr.	HV	...	....	....	....	....	....	79	1	..	..	6	26	23	24	17	3	..	..	..	..	55
	Fasting	Resting	180	45.3	46	24	7.33	17.7	100	2	..	..	10	44	20	16	7	1	..	..	..	..	74
		HV		35.4	18	20	7.66	19.0														
	1 hr.	HV	...	....	....	....	....	....	122	..	..	..	8	27	42	17	6	..	..	..	..	..	77
	End of infusion	HV	...	....	....	....	....	....	342	..	..	..	14	55	22	6	2	..	..	..	..	..	91
L. S. Age: 32	3 hr.	Resting	130	47.9	37	26.5	7.47	20.0	81	10	..	6	14	21	7	14	7	10	7	3	..	..	48
		HV		35.1	16	20	7.71	21.0														
	2½ hr.	HV	...	....	....	....	....	....	85	11	1	7	21	15	12	13	12	7	2	..	..	..	56
	2 hr.	HV	...	....	....	....	....	....	109	15	2	16	45	18	4	..	..	..	..	..	..	..	85
	Fasting	HV	...	....	....	....	....	....	127	14	..	6	35	27	16	3	..	..	..	..	..	..	83
	1 hr.	HV	...	....	....	....	....	....	195	10	4	29	36	16	6	..	..	..	..	..	..	..	90
	End of infusion	Resting	160	47.0	45	25	7.36	19.1	303	15	5	22	31	21	6	..	..	..	..	..	..	..	85
		HV		34.5	17	19.5	7.66	19.5														

J. McM. Age: 26	2½ hr.	Resting	Onset of 2-5/Sec. waves after 120 min. of HV	45.5	36	25	7.46	20.0	83	7	..	..	6	8	15	13	8	13	11	15	5	..	29
		HV		32.7	20	18.5	7.58	21.6																	
	2 hr.	HV		....	....	....	....	....	90	8	..	..	7	16	14	21	14	11	4	4	..	..	37
	1 hr.	HV		....	....	....	....	....	103	2	..	..	8	15	20	7	11	10	14	11	3	..	43
	Fasting	HV		....	....	....	....	....	107	6	..	1	3	8	9	5	7	18	16	20	6	..	21
	End of infusion	Resting	140	43.8	38	24	7.41	20.5	240	12	..	1	18	25	33	9	1	..	..	..	..	..	77
		HV		27.3	11	16	7.77	21.0																	
M. A. B. Age: 57	2½ hr.	Resting	Onset of 2-5/Sec. waves after 100 min. of HV	47.9	37	26	7.46	18.4	84	30	2	3	7	7	1	9	13	16	8	2	..	..	20
		HV		33.0	14	18.5	7.74	19.4																	
	Fasting	HV		....	....	....	....	....	91	24	2	4	24	20	11	6	4	7	..	..	..	..	61
	2 hr.	HV		....	....	....	....	....	93	11	..	9	9	9	6	7	14	23	9	2	..	..	33
	1 hr.	HV		....	....	....	....	....	107	9	3	15	41	27	5	..	..	..	..	..	..	..	91
	End of infusion	Resting	180	49.0	41	26	7.42	17.8	215	51	2	23	17	4	3	..	..	..	..	..	..	..	49
		HV		34.4	14	19.5	7.75	18.4																	
J. P. W. Age: 29	2 hr.	HV¶		....	....	....	....	....	70	32	...	2	11	18	16	12	6	4	..	..	..	..	47
	2½ hr.	Resting	150	44.5	37	24	7.42	18.8	83	28	..	..	8	14	11	8	4	6	5	11	4	..	33
		HV		31.7	15	18.5	7.70	19.4																	
	Fasting	HV		....	....	....	....	....	95	13	..	..	4	19	30	17	7	4	2	3	..	..	70
	1 hr.	HV		....	....	....	....	....	103	23	..	..	4	12	16	21	9	5	4	4	2	..	53
	End of infusion	Resting	150	44.8	44	24	7.35	18.3	265	35	4	8	17	24	11	..	..	..	..	..	..	..	65
		HV		34.2	20	19	7.59	19.0																	
H. W. R. Age: 29	1 hr.	HV		....	....	....	....	....	70	8	..	..	..	3	7	11	11	16	9	16	18	..	10
	2 hr.	HV		....	....	....	....	....	76	9	..	..	..	2	6	11	12	9	15	20	13	3	8
	2½ hr.	Resting	120	48.6	39	29.5	7.43	15.4	82	8	..	..	2	4	9	8	8	13	16	17	12	2	15
		HV		36.6	19	20.5	7.65	16.5																	
	Fasting	HV		....	....	....	....	....	98	2	..	1	4	7	7	14	11	14	15	18	8	..	19
	End of infusion	Resting	140	48.5	46	25	7.35	16.3	163	4	..	1	4	11	18	24	20	10	4	2	..	..	34
		HV		33.6	17	18.5	7.65	16.5																	
R. McM. Age: 25	2½ hr.	Resting	160	45.0	....	....	7.38	21.7	76	26	4	5	3	3	9	9	9	13	11	8	1	..	24
		HV		30.9	....	....	7.69	22.2																	
	2 hr.	HV		....	....	....	....	....	82	31	3	3	7	10	16	11	6	4	3	3	3	..	39
	Fasting	HV		....	....	....	....	....	95	40	18	16	10	10	4	3	1	1	..	..	..	..	58
	1 hr.	HV		....	....	....	....	....	131	39	8	11	8	10	7	5	5	1	..	..	..	..	44
	End of infusion	Resting	...	43.5	....	....	7.40	20.2	289	49	12	22	10	6	1	..	..	..	..	..	..	..	51#
		HV		29.0	....	....	7.57	21.0																	

* Values are listed in order of increasing blood sugar levels. The subjects and the values obtained in the dextrose tolerance tests are the same as those indicated in table 1.

† In this column, HV indicates hyperventilation.

‡ $BHCO_3$ indicates base bicarbonate.

¶ The hyperventilation was poorly done.

‖ The p_H buffer solution used in this instance did check on control determination.

The hematocrit reading was 55 per cent.

4. Disturbances in consciousness tended to correlate with the amount of slow activity and were greatest at low levels of the blood sugar. On the other hand, the subjective symptoms of numbness, tingling and the like, if different at all, were greater at the higher levels of the blood sugar.

Comment.—Blood sugar levels are obviously of the greatest importance in determination of the response of the electroencephalogram to hyperventilation. The mechanism of this action is not clarified by these studies and must await corresponding work on the cerebral blood flow and changes in the oxygen and carbon dioxide contents of arterial and internal jugular venous blood at varying levels of the blood sugar. It is apparent that the electroencephalographic changes are not due to any effect that the changing level of the blood sugar has on the degree of respiratory alkalosis provoked by hyperventilation.

In routine clinical work, caution must be observed in the interpretation of slowing of cerebral activity during hyperventilation if the level of the blood sugar is not known. Until further data are available on the response of the abnormal electroencephalogram to variations in blood sugar during hyperventilation, it is our opinion that while the wave and spike pattern may be considered defintely abnormal, 3 to 5 per second activity may be regarded only as probably abnormal when the blood sugar is above 120 mg. per hundred cubic centimeters and of doubtful significance at lower levels. Age must also be taken into account, since Liberson and Strauss [10] demonstrated that the amount of slow cerebral activity on hyperventilation varies inversely with age.

TABLE 5.—*Effect of Hyperventilation in the Recumbent and the Erect Position on Frequency Spectrums in the Electroencephalogram*

Subject	Blood Sugar, Mg. per 100 Cc.	Position of Subject	Blood Pressure	Pulse Rate	Electroencephalographic Frequency Spectrum, 180 Sec. Hyperventilation, Percentage												Alpha Activity (8-12/Sec.)
					LVF	12/ Sec.	11/ Sec.	10/ Sec.	9/ Sec.	8/ Sec.	7/ Sec.	6/ Sec.	5/ Sec.	4/ Sec.	3/ Sec.	2/ Sec.	1/ Sec.	
G. E.	104	Recumbent	112/ 68	114	2	..	..	8	19	28	16	8	5	5	6	2	..	55
Age: 28		Erect, 22 min.	98/ ?	150	1	..	..		14	16	18	11	16	13	8	3	..	30
	91	Recumbent	116/ 68	114	2	..	..	3	19	16	8	10	13	11	12	6	..	38
		Erect, 24 min.	112/ 90	114	..	..	..	2	9	9	14	11	13	14	18	10	..	20
	103	Recumbent	114/ 68	90	..	..	..	6	14	24	15	12	11	6	9	2	..	44
		Erect, 20 min.	120/ 70	114	..	..	..	4	10	14	16	12	13	9	14	7	..	28
E. B. F.	100	Recumbent	120/ 86	114	2	..	..	5	17	36	15	13	7	3	2	..	..	58
Age: 37		Erect, 30 min.	116/ 84	138	2	..	..	3	9	23	21	12	9	6	12	2	..	35
J. R.	87	Recumbent	125/ 80	90	4	..	..	10	40	11	9	11	9	4	2	..	..	61
Age: 34		Erect, 18 min.	95/ 80	102	2	..	..	6	25	16	6	8	10	16	7	5	..	47
L. S.	122	Recumbent	110/ 80	96	11	4	27	36	19	2	1	..	..	..	..	..	..	88
Age: 32		Erect, 22 min.	134/ 84	132	20	3	19	23	11	11	9	3	1	..	..	..	..	67
M. A. B.	81	Recumbent	121/ 80	90	12	3	6	13	9	6	11	14	18	7	..	..	..	37
Age: 57		Erect, 21 min.	86/ 56	132	10	..	6	11	14	7	11	12	17	9	3	..	..	38
R. McM.	77	Recumbent	120/100	90	30	6	5	5	3	4	8	7	10	13	7	2	..	23
Age: 26		Erect, 13 min.	122/104	114	35	..	2	4	8	3	8	13	7	9	8	2	..	17
H. R.	?	Recumbent	108/ 56	78	16	9	10	23	12	12	10	3	3	4	2	1	..	61
Age: 29		Erect, 18 min.	118/ 80	90	9	1	1	4	6	8	10	8	14	9	13	14	1	20
J. McM.	87	Recumbent	140/ 90	126	3	..	3	18	9	9	9	4	11	12	15	6	..	41
Age: 26		Erect, 24 min.	130/ 90	132	9	..	2	11	7	3	7	13	16	17	11	3	..	23
R. A. K.	105	Recumbent	142/ 90	114	38	..	2	10	20	16	9	3	..	2	..	..	..	48
Age: 42		Erect, 28 min.	95/ 80	150	8	..	1	5	3	4	8	9	16	27	16	2	..	13

As for experimental work, it need only be stated that observations during hyperventilation are without significance unless the factor of the level of blood sugar is controlled.

Posture.—Nine subjects were studied on the tilt table. After they had recovered from three minutes of vigorous hyperventilation in the recumbent position, they were tilted to the erect position, and after thirteen to thirty minutes of motionless standing, they again overventilated

10. Liberson, W. T., and Strauss, H.: Electroencephalographic Studies: Slow Activity During Hyperventilation in Relation to Age, Proc. Soc. Exper. Biol. & Med. **48**:674, 1941.

for three minutes. One channel was used to record the electrocardiogram. The blood pressure was determined frequently before and during hyperventilation. In no instance was there a significant fall in arterial blood pressure due to motionless standing alone.

In all but 2 instances the degree of slowing of the brain waves was significantly greater when the subject was in the erect position than when he was in the recumbent position (table 5; fig. 2 *D*). In a few subjects the difference was striking. In all instances hyperventilation was accompanied by tachycardia, which was always greater when the subject was in the erect position. During hyperventilation there were usually a slight decrease in pulse pressure with the subject in the recumbent position and a more decided decrease when he was in the erect position. In 4 instances the systolic pressure fell to below 100 mm. of mercury. Disturbances in consciousness were greater with the subject in the standing position, but in no instance did muscular relaxation or evidences of impending syncope develop. Three subjects, not included in the present series, hyperventilated first in the erect and then in the recumbent position, with similar results; this observation rules out the possibility that the greater effect noted when the subject was in the erect position was due to incomplete recovery from the first period of hyperventilation.

Comment.—The most obvious physiologic difference in response to hyperventilation in the two positions is found in the magnitude of the circulatory reactions. Cerebral blood flow is known to decrease when the subject hyperventilates in the recumbent position. The magnitude and direction of the observed changes in pulse and blood pressures when the subject is in the erect position are such as to suggest that if any further change in cerebral blood flow is associated with the erect position, it is in the direction of an additional decrease. This circulatory reaction, however, is not the only factor, or even necessarily the most important one, since the degree of change in the electroencephalogram did not correlate well with the magnitude of the changes in the pulse and blood pressures. Indeed, in the instance in which the blood pressure fell to the lowest point the cortical frequency spectrum showed the least change. Another possible factor may be a more effective respiratory exchange when the subject is hyperventilating in the erect position, due to a greater vital capacity. Whatever the mechanism, the results make it clear that posture must be taken into account as a variable in both clinical and experimental studies involving hyperventilation.

GENERAL COMMENT

The method of analysis of cortical frequency spectrums presented in this report provides a simple and practical procedure for quantitating changes in frequency under varying experimental conditions. The method, however, has certain limitations, which must be emphasized. First, as has already been pointed out, the distribution of waves per second, rather than the distribution of wavelengths, is determined. For this reason, waves of certain lengths which are obvious on inspection of the record but which appear in runs of less than one second's duration may not be represented in the spectrum, since they are averaged with waves of the more dominant frequency. While these spectrums are thus not strictly comparable to spectrums for true wavelengths, they are nevertheless of equal value in demonstrating shifts in frequency. In this respect studies using this method and those employing the Grass analyzer [2] have yielded comparable results.

A second criticism is that our method represents an oversimplification of the electroencephalogram in that it ignores the subdominant superimposed and base line oscillations. This need not be a serious obstacle to the detection of significant shifts in frequency, since the results with the Grass analyzer have indicated that while the electrical activity of the cortex is a manifestation of the activity of a great number of chemical oscillators having different natural periods, these oscillators tend to respond to the same factors in the same direction, though not necessarily to the same degree. The present method depends chiefly on the oscillators, which are represented by sine waves to a greater or less degree. Analysis of normal records containing only a small proportion of sine wave activity (i. e., low voltage fast waves or low alpha rhythm) proves difficult during variations within physiologic ranges, but in their shift to abnormal zones there is usually an increase in sine wave activity of slower frequency. This has been demonstrated in studies on delirium,[6] during hyperventilation and during exposure to toxic substances.[11] For the study of borderline changes in normal subjects, however, it is probably advisable to select subjects whose electroencephalograms have a high percentage of alpha activity.

With respect to the influence of various constituents of the blood, our studies confirm Gibbs's data indicating that at least the distribution of frequencies shows a continuous change through normal and supernormal ranges, as well as in

11. Unpublished data.

pathologic ranges.[8] The normal electroencephalogram thus reveals a considerable range in distribution of frequencies within physiologic zones. This observation offers a new approach to the study of the abnormal, and more particularly the borderline normal, electroencephalogram, especially when disturbances in cerebral metabolism may be present. This is of particular value in studies of toxic substances or noxious procedures, in which it is of importance to detect the earliest harmful effects on the central nervous system. By establishing the normal zones of response to physiologic variables in the experimental subjects (fig. 2) one can more readily detect the point at which the noxious experience exceeds the physiologic zone for each subject. It is obvious from the data in this paper alone that the mere presence or absence of delta activity is not an adequate criterion. When the technic is combined with careful psychologic studies of fluctuations in the level of awareness, one has no difficulty in establishing with a high degree of accuracy normal, borderline and pathologic zones. So far we have used this technic successfully in investigations on a number of harmful materials, including alcohol, and on oxygen lack, as well as in a study of clinical delirium due to a wide variety of factors.[8]

SUMMARY

A simple method of determination of the average frequency distribution of the electroencephalogram, which is presented here, yields a spectrum of the average number of waves per second and is highly accurate for regular records, although progressively less accurate with records of decreasing regularity.

After intravenous infusion of dextrose there was a shift toward faster frequencies (up to 12 per second) with rising levels of dextrose in the blood and a shift toward slower frequencies with falling levels of dextrose. The amount of low voltage fast activity, however, was not influenced by the dextrose level in the blood.

Inhalation of 100 per cent oxygen for five minutes or longer resulted in a shift toward faster frequencies (up to 12 per second).

Change from the recumbent to the erect posture had no effect on the cortical frequency spectrum unless orthostatic hypotension developed.

The decrease in frequency of the brain waves during hyperventilation was greatest with low dextrose levels in the blood and least with high dextrose levels in the blood, in spite of comparable alterations in hydrogen ion concentration, carbon dioxide tension, carbon dioxide content and base bicarbonate concentration of the arterial blood.

Hyperventilation produced much greater slowing when the patient was in the erect position than when he was in the recumbent position. Tachycardia and decrease in pulse pressure were also greater when the subject was in the erect position than when he was in the recumbent position during hyperventilation.

Cincinnati General Hospital.

ELECTRODIAGNOSIS BY MEANS OF PROGRESSIVE CURRENTS OF LONG DURATION

STUDIES ON CATS WITH EXPERIMENTALLY PRODUCED SECTION OF THE SCIATIC NERVES

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CHICAGO

In his description of the reaction of degeneration, Erb [1] included as a part of the changes the increase in galvanic excitability. This was a subject of dispute between Vulpian and Erb and Biedermann and Erb.

Erb stated that there was an invariable increase in galvanic excitability, beginning in the second week and lasting as long as two months. Roberts,[2] in experiments on rabbits in which the bare muscle was stimulated, found this to be a constant sign; "about three weeks after nerve section the increased response to the galvanic current . . . is indeed very striking." In his experience in clinical work the results obtained were less constant.

Employing percutaneous bipolar stimulation, we have found that two weeks after section of the sciatic nerve in the cat the liminal amount of current is small, usually below 1 milliampere —at times of the order necessary to stimulate the normal muscle but frequently less. In our experiments the first electrical examination was made fourteen days after section to prevent injury to the degenerating muscles.

This low threshold for galvanic stimulation persists for a long time. In completely denervated muscles, large portions of the sciatic nerve having been removed and absolute alcohol having been injected into the proximal and distal ends to discourage regeneration, we observed this low threshold to persist as long as our experiments were continued, for two hundred and eighty-two days (fig. 1). In animals in which the sciatic nerves were sectioned and the ends looped back and sixty days later the ends resected and sutured, we also noted this low threshold to galvanic stimulation during the sixty days preceding secondary suture. In animals in which the sciatic nerves were sectioned and the ends immediately sutured, we observed the same lowered threshold to galvanic stimulation for a certain number of days, varying from thirty-seven to sixty, when, either before or coincident with motor signs of recovery, the minimal amount of current necessary to produce a contraction suddenly increased and diminished only later, remaining high for as long as one hundred and twenty days (fig. 2).

We wish here to call attention to the confirmation of Erb's observation of the existence of a low threshold of excitability to galvanic stimuli after complete section of a nerve and to its persistence for as long as our denervated animals were observed, two hundred and eighty-two days. We particularly wish to mention the sudden increase in the threshold to galvanic stimulation immediately before, and at times just when, motor signs of successful neurotization occur. We call attention to this increase since a related phenomenon in the response of denervated muscles to progressive currents has been described and is confirmed by us, and since in cats at least positive indication of successful neurotization may be obtained by means of such currents.

The relation existing between the rate of variation in current and the minimal strength of current required to produce excitation has been investigated by physiologists for many years, since an attempt was made to study it by Du Bois-Reymond [3] in 1862. Bernstein,[4] von Fleischl,[5] von Kries,[6] Fick,[7] Schott [8] and Gildemeister [9] were among the older investigators.

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The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Northwestern University.

1. Erb, W.: Deutsches Arch. f. klin. Med. **4**:535-578, 1868.

2. Roberts, F.: Brain **39**:297-347, 1916.

3. Du Bois-Reymond, E.: Abhandl. d. k. Akad. d. Wissensch. zu Berlin, 1862, pp. 75-163.

4. Bernstein, J.: Arch. f. Physiol., 1862, pp. 531-532.

5. von Fleischl, E.: Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. cl. **76**:138-162, 1877.

6. von Kries, J.: Arch. f. Physiol. **8**:337-372, 1884.

7. Fick, A.: Beiträge zur vergleichenden Physiologie der irritabelen Substanzen, Braunschweig, F. Vieweg u. Sohn, 1863.

8. Schott, J.: Arch. f. d. ges. Physiol. **48**:354-385, 1891.

(Footnote continued on next page)

Such so-called progressive currents as have been studied may be divided into linearly increasing, or progressive, currents and exponentially increasing, or progressive, currents.

Among the more recent investigators to whom more accurate methods of measurement have been available and who have studied exponentially rising currents may be mentioned Liberson,[10] Schriever,[11] Delville,[12] Cardot and Laugier,[13] d'Hollander,[14] Solandt [15] and Fabre.[16] In these experiments the duration of rise of the exponentially increasing current to its peak was less than one second—often fifty to two hundred milliseconds. In the more recent experiments on linearly increasing, or progressive, currents, the longest period likewise was usually less than one second—in the case of Lucas [17] one and two-tenths seconds. From these experiments certain predictions were made in relation to the response of muscle and nerve to progressive currents of long duration which have not been confirmed by our work. Certain formulas and constants have been derived from the experiments with currents of relatively short duration which we feel will require some modification, but with which we are not concerned at this time. In 1907 Lucas published the results of his studies on the sciatic nerves of the toad and frog and on the sartorius muscle of the frog. He found that the minimal rate of rise, which he called the minimal current gradient, in the case of the toad was of such an order that the liminal strength at instantaneous stimulation would have to be increased 46 times at the end of a second to produce an effective stimulus; for the sciatic nerve of a frog, the minimal strength at instantaneous stimulation would have to be increased 63 times at the end of a second to be an effective stimulus. Among his conclusions is the following statement:

> It is found that as current gradient is decreased the current strength required for excitation increases more and more rapidly until a definite minimal gradient is reached. No gradient less steep than this will excite.

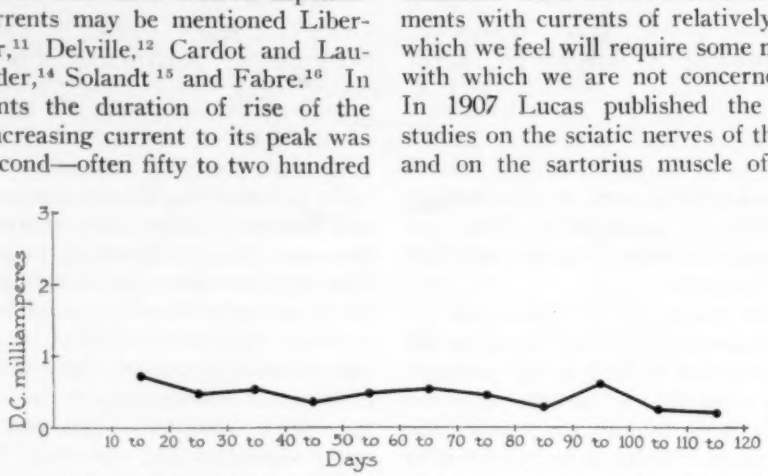

Fig. 1.—Average milliamperage necessary to produce an adequate stimulus by bipolar anodal closing stimulation at various days after denervation.

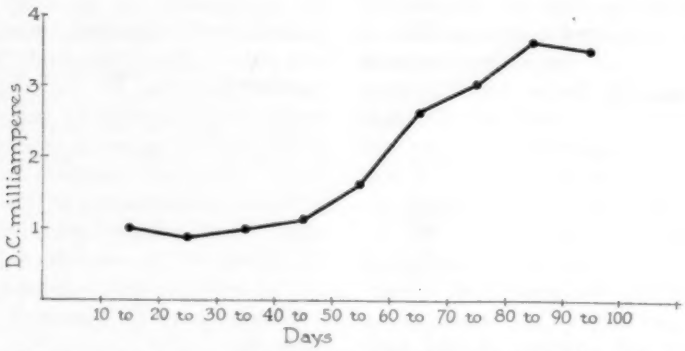

Fig. 2.—Average milliamperages necessary to produce an adequate stimulus by unipolar anodal closing stimulation at various days after primary suture.

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15. Solandt, D. Y.: Proc. Roy. Soc., London, s.B **119**:355-379, 1936.

16. Fabre, P.: Compt. rend. Acad. d. sc. **185**:300-302, 1927.

17. Lucas, K.: J. Physiol. **36**:253-274, 1907-1908.

The belief that progressive currents possessing less than a minimal rate of rise will not stimulate even though they finally reach a considerable value was likewise expressed by Hill.[18] From Lucas' experiments, Blair [19] reached the conclusion that "when the gradient is too low for the rheobase to be effective no voltage is effective."

In an analysis of Solandt's [20] data obtained from stimulation of the frog's sciatic nerve with exponentially rising currents, it may be seen that with a minimal gradient the current increases at a rate such that a value 16.7 times the rheobase value is reached in 0.27 second.

We found when using linearly increasing currents of longer duration—1.2, 2.6, 3.8 and 8.8 seconds—that the aforementioned liminal gradients did not exist for all times. One graph (fig. 3) may suffice to illustrate the point. In the case of the normal muscle, the liminal current

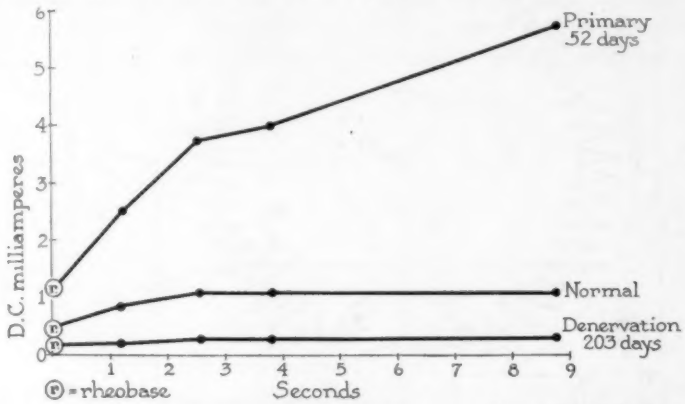

Fig. 3.—Comparison of milliamperages necessary to produce an adequate stimulus with progressive currents of various durations after a primary suture and in a normal and a denervated muscle.

at instantaneous stimulation, or the rheobase, was 0.4 milliampere; at 1.2 seconds the current was 0.8 milliampere, or twice the rheobase; at 2.6 seconds, 1.05 milliamperes, or 2.62 times the rheobase; at 3.8 seconds, 1.1 milliampere, or 2.75 times the rheobase, and at 8.8 seconds, 1.15 milliamperes, or 2.87 times the rheobase. At no time was the rheobasic current adequate to stimulate; yet with a current of long duration, 8.8 seconds, an increase of only 2.87 times the rheobase was an effective stimulus. We observed that there is a relatively liminal gradient for each particular time in which the peak of the current is reached. When at that current gradient a contraction begins at, say, 3.8 seconds and the current is allowed to increase linearly to 8.8 seconds, a tetanic contraction persists as long as the current is allowed to increase progressively at that particular rate of change. While we shall postpone our explanation of these observations until a later communication, we wish to report on the differences observed in completely denervated muscle, recovering muscle and normal muscle.

Electrodiagnosis and electrotherapy by means of currents having various wave forms have been studied for many years. These studies include investigations on condenser discharges; faradic currents, when applied suddenly and interrupted suddenly, and when applied in a slowly increasing and decreasing wave form, as described by Bergonie [21]; variations of square wave galvanic currents of varying periods, such as the le Duc current, and, finally, unidirectional sinusoidal currents, alternating currents, linearly progressive currents and exponentially increasing currents. The last four types of currents are of interest in relation to our work.

In earlier years the impetus for development of new wave forms of stimulation was the desire to imitate the normal contraction of a muscle and to avoid the abrupt movement produced by sudden closure of a current, whether faradic or galvanic (Bergonie). In 1907 Bordet [22] described an apparatus for the production of a galvanic wave current lasting as long as 2.5 seconds. With regard to diagnosis, he noticed that when a muscle is degenerated the time necessary to reach a current adequate for stimulation is long as compared with that necessary for normal muscle, with which the liminal current must be reached more quickly. For similar reasons, Laquerrière [23] designed a new apparatus on the basis of the work of Bergonie. In

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19. Blair, H. A.: J. Gen. Physiol. **15**:731-755, 1931-1932.

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22. Bordet, E.: Arch. d'électric. méd. **15**:452-461, 1907.

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1912 Becker [24] described an apparatus called a myomotor, which delivered saw tooth waves. In 1931 Delherm and Laquerrière [25] described an apparatus which delivered alternating currents of long duration and unidirectional galvanic wave forms. The currents described by Bordet, Laquerrière and Delherm have been designated by Duhem [26] as currents of long period, to distinguish them from currents described by d'Arsonval in 1891 and by Lapicque,[27] who, without knowledge of the work of d'Arsonval,[28] published the results of his studies in 1915.

Whereas the currents designated as those of long period may last several seconds, those designated as progressive currents by Delherm last only a fraction of a second. From the standpoint of their contribution to diagnosis, it is said of both types that a degenerated muscle will respond to the condition in which a liminal current is reached more slowly, whereas with the normal muscle this amperage must be reached more quickly.

Although many articles in the literature are concerned with progressive currents of long period (more than two seconds), the clinical material from which data have been obtained is small. No accurate measurements of time and current are described, and no experimental work is recorded.

It is necessary, we believe, better to define a progressive current. We take such a current to be one which increases with time. The kind of progressive current is determined by its wave form—for example, whether linear, exponential or sinusoidal.

The progressive current used in these experiments was a linearly increasing one, consisting of the ascending limb of a unidirectional galvanic wave of isosceles triangle type. The decision to use a current wave of this type in preference to a saw tooth wave was based on several considerations. In the first place, one is able to observe a contraction at the peak of the wave. Also, one is able to obtain simultaneous readings of the voltage and strength of current at the instant of the contraction. In addition, one is spared the confusion resulting from unwanted break contractions, which are likely to occur with the saw tooth wave.

The generation of the wave of the isosceles triangle type is dependent on the operation of a specially constructed potentiometer, the moving

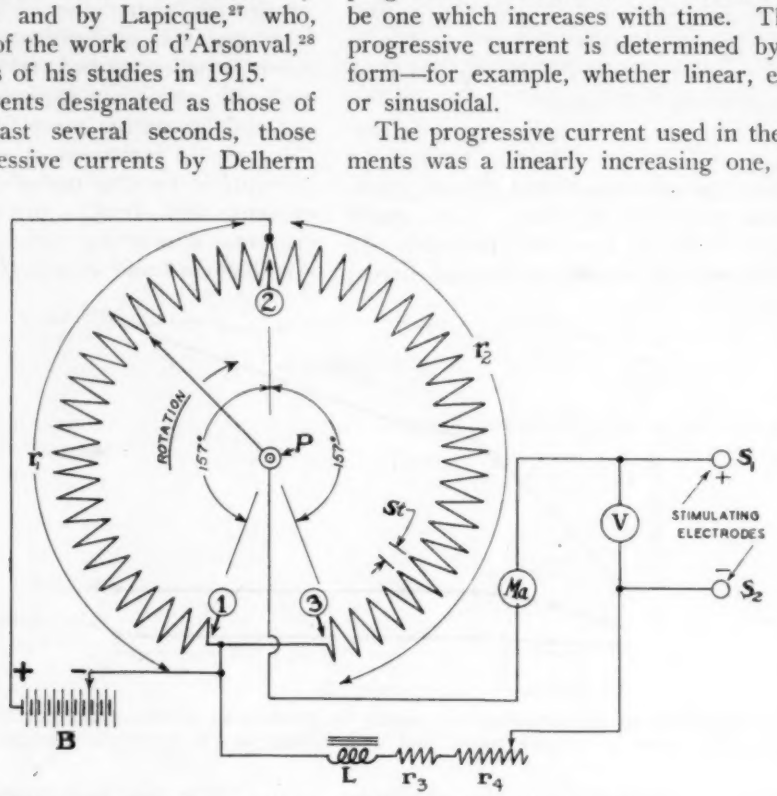

Fig. 4.—Circuit diagram of the apparatus for production of progressive currents.

In this diagram, r_1 and r_2 indicate the potentiometer, with a resistance of 400 ohms; r_3 is the fixed resistor, with a resistance of 1,000 ohms; r_4, the rheostat, with a resistance of 100,000 ohms; L, the choke coil, with an inductance of 30 henrys and a resistance of 130 ohms; St, a step, or the distance between adjacent turns of wire, r_1 and r_2 equaling 600 steps; B, the storage battery; Ma, the milliammeter, and V, the voltmeter, with a resistance of 5 x 10^6 ohms. All resistors are wound with wire.

24. Becker, W.: Ztschr. f. phys. u. diätet. Therap. **16**:583-600, 1912.

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27. Lapicque, L.: Compt. rend. Acad. d. sc. **161**:643-646, 1915.

28. d'Arsonval, A.: Compt. rend. Soc. de biol. **3**: 283-286, 1891.

arm of which may be continuously rotated through multiples of 360 degrees at various predetermined, constant rates. This moving arm is driven through suitable worm and spur gear reduction units by means of a shaded pole, 60 cycle induction motor, the speed of which is held constant by a centrifugal governor. A ripple-free, unidirectional current is supplied to the potentiometer from a low resistance storage battery, the output of which could be varied in 2 volt increments from zero to 36 volts. This primary current enters the center tap (point *2*) of the potentiometer winding and passes out through the junction between the initial and the final turn (points *1* and *3*) of this winding (fig. 4).

A secondary current, which shall be called hereafter a progressive current, emerges from the moving arm of the potentiometer and passes through an external series circuit, consisting of a milliammeter, the specimen, a variable resistor, a fixed resistor and a choke coil. The milliammeter has been placed in the circuit to measure the current actually passing through the specimen. Although the voltmeter is located across the stimulating electrodes, the current which passes through it is truly negligible. The variable resistor, r_4, enables one to obtain continuously adjustable maximums of current, from about 0.125 to 15 milliamperes, and it assists in maintenance of linearity in the current wave, though the specimen may be changing in resistance during the examination.

The fixed resistor, r_3, which has a value of 1,000 ohms, is always kept in the circuit to assure linearity, even when r_4 is reduced to a low value. The choke coil is used to smooth out the small, but unavoidable, step effect which is created as the moving arm of the potentiometer passes from one turn of the resistance winding to the adjacent turn.

In this discussion, the terms 1.2, 2.6, 3.8 and 8.8 second times mean that 1.2, 2.6, 3.8 and 8.8 seconds respectively are required for the progressive current to reach its maximal value.

Because of the inertia of the galvanometer, there was an appreciable difference between the dynamic and the static values for the current and the voltage at the faster times. For example, at the 1.2 second time the dynamic value of the current was 0.9 milliampere and the static value 1.02 milliamperes. At the 2.6 second time the dynamic value was 1.02 milliamperes and the static value 1.05 milliamperes. At the 3.8 second time the dynamic value was 1.03 milliamperes and the static value 1.05 milliamperes. At the 8.8 second time the dynamic value was 1.05 milliamperes and the static value 1.06 milliamperes. There was a corresponding difference in the dynamic and the static values for the voltage.

Figure 5 shows that 1.1 milliamperes was the average strength of current required to produce a minimal contraction in 25 normal specimens at the 3.8 second time. For a progressive current of this value it was possible to have the total resistance of the external circuit at a value slightly greater than 27,000 ohms. This fact is emphasized because the accompanying cathode ray oscillogram (fig. 6) showed excellent linearity of the wave when the total resistance of the external circuit was only 1,000 ohms and the maximal value of the progressive current was as high as 10 milliamperes.

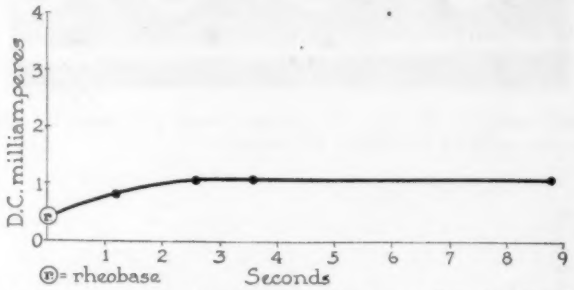

Fig. 5.—Median of the milliamperages necessary to produce an adequate stimulus with progressive currents of various durations in 25 normal animals.

Before the examination, the site over which the electrodes were to be placed was first pricked deeply by a needle five times and vigorously rubbed with electrode jelly to minimize cutaneous resistance; the indifferent electrode, measuring 2 cm. in diameter, was placed over the lateral portion of the achilles tendon. The exploring electrode, the anode, measuring 1.5 cm. in diameter, was placed in the middle and lower part of the popliteal fossa. The electrodes, which were circular, were constructed of copper and covered with chamois; they were immersed in salt solution for fifteen minutes prior to use and then covered with electrode jelly. When a rheobase was to be determined, the choke coil was shunted out of the circuit.

In addition to studies of linearly increasing progressive currents, we studied the effect of alternating currents and half-wave rectified alternating currents of very low frequencies, 90 degrees of which last 0.33, 0.5, 1 and 3 seconds, with frequencies of 0.75, 0.5, 0.25 and 0.083 cycles per second respectively. For practical clinical purposes, the results with both types of current were comparable.

The data already described for normal muscle were characteristic for all the animals studied (fig. 5).

Within a few days after denervation, the amount of current necessary to excite the muscle by progressive currents of long duration was usually somewhat higher than the amount required by the normal muscle. It began to diminish after about twenty days, and between thirty and forty days it was less than normal and remained so as long as the animals were studied (fig. 7).

In denervated muscles, whether during the period prior to neurotization, in the case of primary sutures, or before suture was done sixty days after section, or after a large portion of the sciatic nerve was removed and injection of absolute alcohol made into the proximal and distal ends to discourage regeneration, there was a response to very small currents whatever the gradient may have been. Thus, it was seen that as long as two hundred and three days after denervation, the rheobasic current being 0.18 milliampere, contraction occurred at 8.8 seconds with 0.27 milliampere (fig. 3).

Von Kries [29] stated that in curarized muscle of the frog the same strength of current was required to produce stimulation in 0.125 second as was needed for instantaneous stimulation. Lucas found this to be true of the nerve-free pelvic end of the uncurarized sartorius muscle of the toad. However, he attributed the response to the local cathodic contraction, and when he recorded the occurrence of a conducted contraction, he found that the strength of current had to be increased as the time of increase in current became longer.

In our experiments, because of the critical movement in the foot and toes on stimulation and the continued tetanus occurring when at any particular gradient the current was allowed to increase for longer periods, we believe the contraction was a conducted one.

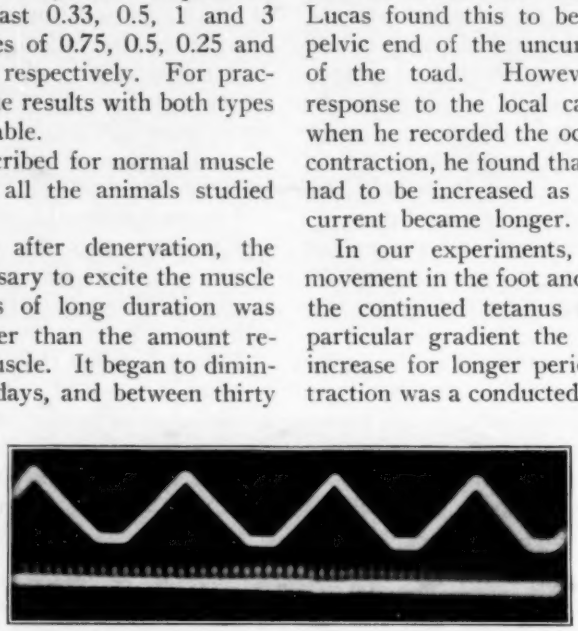

Fig. 6.—Cathode ray oscillogram of the isosceles triangle wave generated by the progressive current apparatus. The interval between the markers represents 0.2 second.

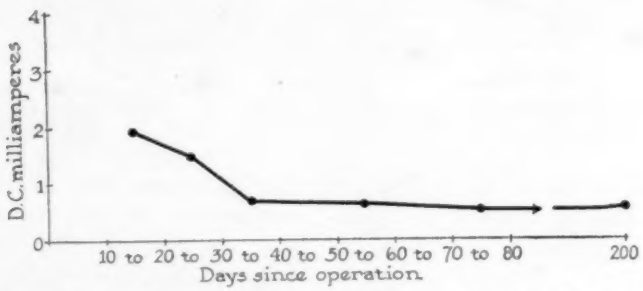

Fig. 7.—Average milliamperage necessary to produce an adequate stimulus with a progressive current of 3.8 seconds' duration in 15 denervated animals at various days after operation.

In contrast to the period of denervation, at times before, and sometimes coincident with, evidence of motor return, the amount of current necessary to produce excitation must be increased considerably above the rheobase when the current is allowed progressively to increase for long periods. Thus, in figure 3, four days prior to the recorded examination made fifty-two days after primary suture the muscle reacted as a denervated one. On the fifty-second day the rheobase was 1.15 milliamperes; at 1.2 seconds contraction occurred with 2.5 milliamperes, at 2.6 seconds with 3.75 milliamperes, at 3.8 seconds with 4 milliamperes and at 8.8

29. von Kries, J., cited by Lucas.[17]

seconds with 5.75 milliamperes. As regeneration progresses, the amount of current necessary for excitation becomes even greater, and a normal pattern is not reached even when fairly good motor recovery has taken place (fig. 8).

In describing the response of muscles possessing a long chronaxia, Lapicque stated in effect that, given a progressive current of a constant rate of increase, diminution of this rate leads to a slight diminution of efficacy of stimulation. This, as has been seen in our experiments, is true only for completely denervated muscles. When, however, neurotization occurs, and for months afterward, and during periods when the chronaxia of the muscle is far longer than that of normal muscle, increasingly large currents are required to excite the muscle when the duration of the progressive current wave becomes longer and longer or the gradient lower. The response of muscles to progressive currents of long duration is not related in all cases to the chronaxia of the muscle.

We wish to call attention to another difference in the responses of regenerating, denervated and normal muscles to progressive currents. As is well known, when after a galvanic current is passed through a frog's muscle by closure of the circuit with contraction of the muscle, repeated opening and closing of the circuit or long-continued passage of stronger currents results in the closing stimulus becoming ineffective, supposedly because of electrotonus. This "electrotonus" effect may be observed to a conspicuous degree after repeated stimulation with a progressive current in regenerating muscle, to a far less degree in denervated muscle and to a minimal degree in the normal muscle of a cat.

Thus, in a normal muscle a contraction produced at the peak of a progressive current continued to be obtained each time the stimulus was repeated, without any rest, as long as the effect was studied (twenty-five times) at the same amperage. When large continuous currents were passed through the muscle, the passage of a progressive current immediately afterward produced a contraction at its peak, as it did before stimulation with the polarizing current.

In the case of denervated muscle repeated liminal stimulation may be effective at least ten times, whereas in the recovering muscle only the first one or two stimuli are effective. It is true that the liminal amperage is greatest for the recovering muscle, less for the normal muscle and least for the denervated muscle. In the recovering muscle, when the liminal strength of current necessary to produce contractions at the peak of a progressive current lasting 1.2 seconds was 6.4 milliamperes, repetition of the stimulus was effective only four times.

When at this same amperage and time a denervated muscle was stimulated repeatedly, the stimuli were effective one hundred times, and the same results were obtained for the normal muscle. In the case of the denervated muscle a fatigue-like effect was noticed in that the strength of the contractions diminished with repeated stimuli more than it did in the case of the normal muscle.

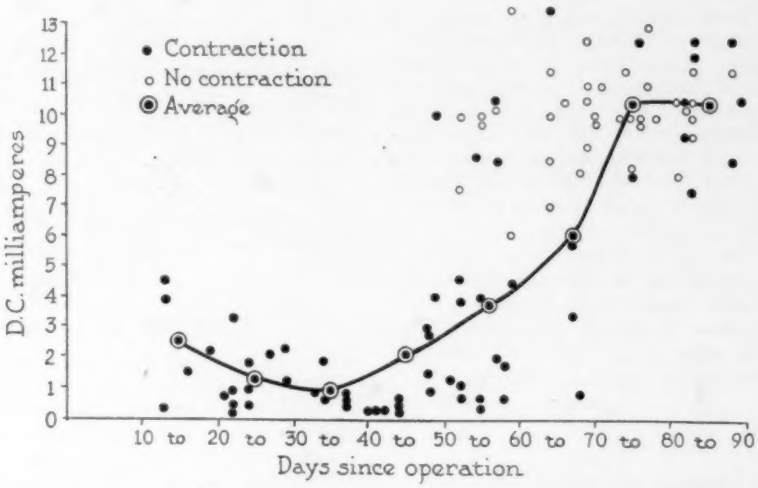

Fig. 8.—Spot graph and average milliamperage necessary to produce an adequate stimulus with a progressive current of 3.8 seconds' duration in 30 animals with primary sutures at various days after operation.

SUMMARY

The denervated muscle prior to neurotization may be made to contract by stimulation with an increasing, or progressive, current of very small amperage whatever the current gradient may be.

When neurotization occurs, the current necessary for excitation must be progressively increased the longer the duration of the current or the less steep the gradient.

For normal muscle, at different times, different current gradients must be reached, but no one liminal gradient exists for all times.

CONCLUSIONS

1. The denervated muscle responds to instantaneous galvanic stimuli of very low amperage for at least two hundred and eighty-two days.

2. The denervated muscle responds to a progressive current of long duration at very low amperage irrespective of the current gradient for as long as two hundred and eighty-two days.

3. To excite the neurotized muscle with instantaneous stimuli a much greater current is required.

4. When a successful junction between the regenerating nerve and the muscle has been effected, there is a sudden, pronounced increase in the amperage necessary to produce excitation with progressive currents. The longer the duration of the progressive current, the greater the strength of current necessary to produce excitation.

5. In the normal muscle the minimal current adequate for excitation by progressive currents differs for each long period, or time constant, but there is no liminal current gradient for all durations.

BIOPSIES OF THE BRAIN OF SCHIZOPHRENIC PATIENTS AND EXPERIMENTAL ANIMALS

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MANTENO, ILL. CHICAGO

Despite the multitude of investigative activities, the question of the histopathology of schizophrenia has remained controversial to date. Perhaps one of the factors contributing to this situation may reside in the well known difficulties associated with the procurement of case material from which valid conclusions can be drawn.

Accessibility to a comparatively large amount of case material, free of complicating factors, such as old age, chronic intercurrent disease, and changes in the brain before, during or after death, would therefore afford one the unique opportunity to contribute to the clarification of the problem. Material selected under such advantageous conditions was found in specimens from the brains of schizophrenic patients obtained for biopsy during prefrontal lobotomy. The patients could be freely chosen for that procedure with regard to age and health. Moreover, the patients were not physically ill at the time the specimens were taken, and a minimum of time elapsed between removal of tissue and fixation.

MATERIAL AND METHOD

Fifteen patients with a condition diagnosed as schizophrenia were selected for bilateral prefrontal lobotomy. Microscopic examination of specimens of the brain of only 12 of the 15 patients will be discussed here, since the results for 3 patients who were over 50 years old may have been related to their age and inclusion of such data might thus yield erroneous conclusions. The changes in the brain of other patients (case 1) appeared to be on an inflammatory, rheumatic basis, and the data were therefore discarded for final evaluation of cerebral changes associated with schizophrenia. The ages of the remaining 11 patients varied from 25 to 50 years, with an average of 35 years; the average duration of the disease for this group was fourteen and seven-tenths years. Throughout examinations, including roentgenographic studies, blood counts and urinalyses, established the presence of perfect physical health, except in the single case just mentioned.

Through burr holes and after crucial incision of the dura, biopsy specimens about the size of a pea were removed from the cortex of the right and of the left prefrontal area before actual leukotomy was performed. Specimens were preserved in 70 per cent alcohol, a 10 per cent concentration of solution of formaldehyde U. S. P., Zenker's fluid and Cajal's bromide–solution of formaldehyde–ammonium solution. Pyroxylin blocks were used for toluidine blue stains, and frozen sections were prepared with sudan III, Cajal and Penfield stains. Myelin sheath stains, Bielschowsky impregnations and hematoxylin-eosin stains were carried out on paraffin-embedded material. Sections obtained from normal persons who had died suddenly after injury were used as controls.

The lobotomy was performed with the use of pentobarbital sodium and general anesthesia on 1 patient and with ether anesthesia on the remaining patients. Since the ether narcosis could have produced the changes observed, provision of controls was imperative. Such controls were found in the brain of 2 patients who had died during general surgical procedures while under ether narcosis. Furthermore, the specimens of the brain of the patient (case 2) who was operated on while under anesthesia induced by local and intravenous administration of pentobarbital sodium served as an additional control for the possible eventuality of changes due to ether. As a complementary control, biopsies were made of the brains of experimental animals (cats and rats) at various intervals during prolonged ether narcosis, lasting from one to six hours.

Of the 15 patients, 3 died shortly after the operation, a circumstance which provided us with the opportunity of comparing the results of the previous biopsies with those of examination of the whole brain and substantiated the biopsy observations. One of these patients, aged 50, showed conspicious arteriosclerotic changes. His case therefore was included with 4 cases which were held unsuitable for an evaluation pertaining to the scope of this study.

RESULTS

Table 1 indicates the patients' ages at the onset of mental illness and at the time of operation. It lists the most important diseases the patients had undergone and, in a separate column, states whether the patient had previously received shock therapy.

CASE 1.—Biopsy of a specimen of the brain of this patient, a woman aged 25 with typical schizophrenia, revealed indubitable organic changes. However, she was observed to have rheumatic heart disease, and a systolic murmur was heard over the apex at the time of the operation. Many ganglion cells were filled with fat droplets. The presence of fat-containing glia cells indicated transport of fat into the adventitial spaces of the smaller vessels of the brain, the walls of which contained considerable deposits of fat in the media and the intima. Toluidine blue preparations showed scattered regions of vacuolar degeneration and shrinkage of the ganglion cells. Isolated areas revealed hypertrophic glia cells and *Gliarasen*.

The patient died five days after lobotomy, of bronchopneumonia. Microscopic examination of the entire brain confirmed the observations at biopsy. The chronic recurrent rheumatic endocarditis and myocarditis were

From Manteno State Hospital (Dr. Kirschbaum) and Chicago State Hospital (Dr. Heilbrunn).

Read at the Annual Meeting of the American Psychiatric Association, Detroit, May 10 to 13, 1943.

apparently the cause of the changes noted in the brain. Large areas exhibiting complete loss of neuron cells were visible around small cortical arteries. In the proximity of these areas of paling various forms of degeneration of ganglion cells and increase in fibrous glia cells were evident. Signs of an inflammatory mesodermal reaction were not demonstrable. The case presented a chronic parenchymatous process in the brain, based on vascular disease.

Bruetsch [1] discussed in detail the relation between the changes in the "rheumatic brain" with recurrent endocarditis and the schizophrenic process and emphasized the difficulty associated with identification of the role of the respective processes. In accordance with Bruetsch, therefore, we venture no conclusions with respect to the histopathology of dementia praecox from the observations in this case.

Case 2.—A woman aged 37 was admitted to the institution at the age of 25 with persecutory delusions, visual and auditory hallucinations and periods of excitement. Later she became fearful and mute, and on occasion she attacked other patients. The results of physical examination were essentially noncontributory. In 1937 she was given a series of metrazol treatments, without beneficial results. Lobotomy was performed, with the patient under anesthesia induced by local and intravenous administration of pentobarbital sodium. Biopsy of specimens from the brain revealed fat droplets in the ganglion and glia cells, moderate increase of the cytoplasmic glia cells and no alteration of the oligodendrocytes. The toluidine blue preparations showed that the ganglion cells were normal in appearance except for some cells which were swollen and contained vacuoles in the cytoplasm. A few fat-containing adventitial cells were seen in engorged vessels.

Case 3.—A woman aged 38 with a condition diagnosed as schizophrenia died five days after frontal lobotomy. The psychotic behavior of this patient had been characterized by auditory and visual hallucinations, inappropriate laughter, untidiness, impulsiveness and muteness. As in the preceding case, biopsy of specimens of the brain revealed organic changes, manifested by prominent infiltration of fat in the ganglion and glia cells. There were a few fat-laden cells in the adventitia and deposits of fat in the cells of the intima and media of the smaller arteries. In addition, the toluidine blue preparations showed scattered vacuolation and shrinkage of neuron cells, hypertrophy of cytoplasmic glia cells and an increased number of astrocytes. Death resulted primarily from a massive hemorrhage into the right frontal lobe and the ventricles. The question whether or not small infiltrations around vessels in the substantia nigra and the neuronophagia in the nuclei around the third ventricle could be attributed to an independent degenerative process or to the preceding lobotomy and hemorrhage in the brain substance remained unanswered.

Case 4.—A woman aged 35 had the onset of mental illness after her first pregnancy, at the age of 23. The patient expressed many delusions and hallucinations; she stated she felt the influence of machines, roentgen rays, etc., and she had frequent periods of excitement and violence. She screamed frequently. The results of physical examination were essentially without significance.

Toluidine blue stains of pyroxylin-embedded material showed slight changes in the neuron cells of the third layer. A few *Gliarasen* and empty spaces

Table 1.—*Clinical Data on Eleven Patients with Schizophrenia Who Underwent Lobotomy*

Case	Sex	Age at Onset of Mental Illness, Yr.	Age at Time of Operation	Past Illnesses	Age of Occurrence	Shock Therapy
2	F	25	37	.....	.....	Metrazol, 3 yr. prior to operation
4	F	23	35	Scarlet fever; mumps; chickenpox; measles	Childhood	None
5	F	24	28	"Puerperal psychosis"	22	Metrazol, 4 yr. prior to operation
6	F	21	39	Whooping cough; measles; "some infectious diseases"	Childhood 14	None
7	F	21	40	.....	.....	None
8*	F	26	38	Scarlet fever; measles; influenza	2, 14	Sulfur in oil, 6 yr. prior to operation
8	M	18	50	.....	.....	None
9	F	21	37	Asphyxiation for 15 min..... Bronchopneumonia	At birth 34	None
10	F	19	33	Measles and influenza.....	Childhood	None
11	F	19	36	Lobar pneumonia with empyema	27	None
12	F	20	26	Diphtheria; scarlet fever; chickenpox; mumps; tonsillitis; mastoiditis	Childhood	Insulin and metrazol 3 yr. prior to operation

* Patient died five days after lobotomy.

Toluidine blue stains of pyroxylin-embedded material showed slight changes in the neuron cells of the third layer. A few *Gliarasen* and empty spaces

1. Bruetsch, W. L.: Chronic Rheumatic Brain Disease as Possible Factor in Causation of Some Cases of Dementia Praecox, Am. J. Psychiat. **97**:276, 1940.

(*Lückenherde*) were present. The neuron cells contained minute quantities of fat. The cytoplasmic glia cells, while proliferated, were free from fat droplets. A few cells of the arterioles showed infiltration with fat. Slight serous exudation into the perivascular spaces

The toluidine blue stain disclosed pyknosis and shrinking as well as loss of ganglion cells. The dendrites were visible over unduly long distances, the apical dendrites showing corkscrew formation. The cytoplasmic glia cells revealed proliferative changes. Their

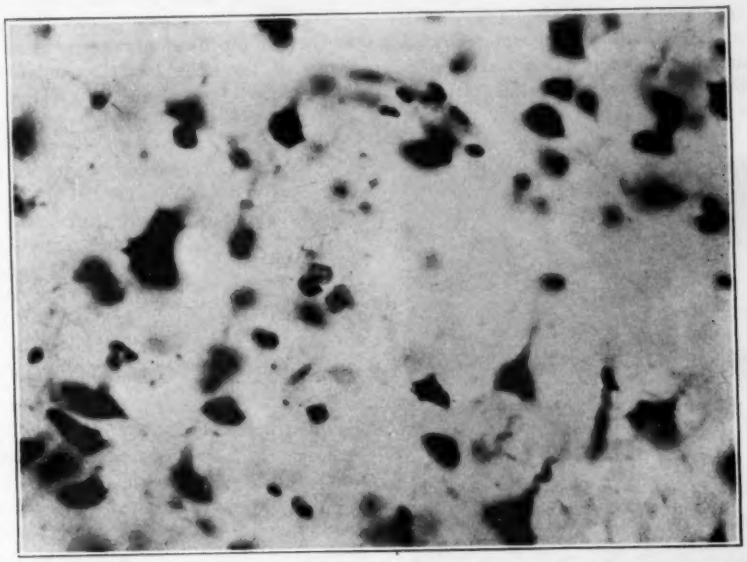

Fig. 1 (case 5).—Biopsy specimen of the frontal lobe, showing enlarged glia cells in the third cortical layer, clusters of glia cells and twisted apical dendrites of degenerated neuron cells (toluidine blue stain; pyroxylin-embedded material).

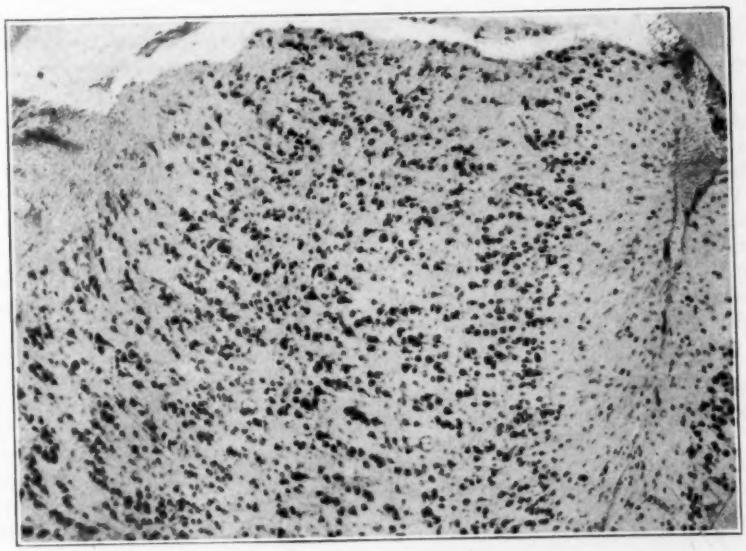

Fig. 2 (case 6).—Portion of a typical biopsy specimen of the frontal lobe, showing slight losses of neuron cells in the third layer, in the upper half of the picture (toluidine blue stain; pyroxylin-embedded material).

was manifest. Myelin sheaths and neurofibrils showed no pathologic change.

Case 5.—A woman aged 28 began to hear voices after childbirth, at the age of 22. She became talkative and unmanageable and struck her baby. For many years she was disturbed, restless and aggressive. There were no pathologic physical signs. Her condition remained unimproved after a course of metrazol injections.

nuclei were enlarged, indented and slightly lobulated. These cells lay isolated or in clusters of four or six (*Gliarasen*). The fibrous astrocytes were increased in number. The oligodendrocytes were slightly swollen. There was infiltration of the neuron cells with minute fat droplets, but none in the small vessels.

Case 6.—A woman aged 39 had the onset of the psychosis at the age of 21. She uttered ideas of

persecution, said she had been poisoned, had periods of excitement, heard the voice of the Lord, laughed in a silly fashion, disregarded her surroundings and became generally withdrawn, but at times was suddenly overactive and violent. There were no physical abnormalities.

The toluidine blue stain revealed among apparently normal neuron cells a few with deeply stained nuclei and cell bodies; some showed vacuolation and swelling, with increased satellitosis; others had disintegrated into mere cell shadows. The cytoplasmic and fibrous astrocytes were increased in number and size. Some of the nuclei were swollen and slightly indented. Fat droplets were discernible in the ganglion cells, as well as in the astrocytes. The presence of minute fat droplets in cells accompanying the axis-cylinders might indicate disturbance of the myelin sheaths. Myelin stains, however, failed to show any abnormality. The adventitial spaces of several small vessels were filled with fat-laden cells. The intima and the cells of the vessel walls showed infiltration with fat.

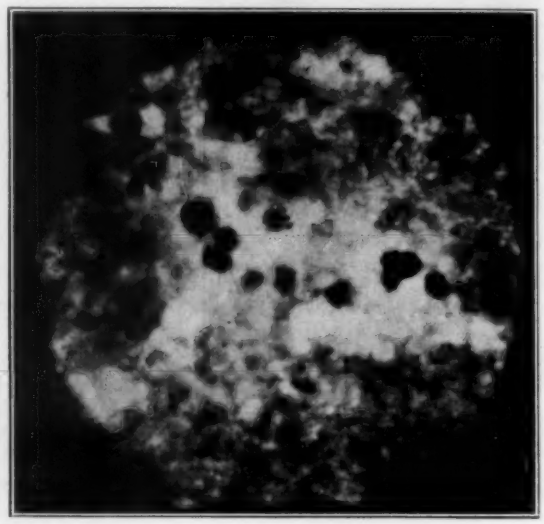

Fig. 3 (case 6).—Fat-laden compound granule cells in the adventitial spaces of arterioles of the brain (sudan III–hematoxylin stain; frozen sections).

Case 7.—A woman aged 40 had the onset of her mental illness at the age of 21; she worried a great deal, had spells of crying and laughing and talked incessantly. She imagined she heard voices and showed mannerisms. She was occasionally untidy, finally became completely out of contact and at times was suddenly violent. Her physical condition was essentially normal.

The ganglion cells, predominantly those of the third and fifth layers, revealed moderate infiltration with fat. The cytoplasmic astrocytes showed a moderate degree of proliferation. The cells and endothelium of the vessels contained deposits of fat. In the adventitial spaces were a few fat-containing compound granular cells. No toluidine blue stains were made, since all the material had been used for frozen sections.

Case 8.—A man aged 50 was first admitted to a state hospital at the age of 20. Prior to this admission he sat around idle for hours, attacked his brother without reason, ran away, took off his clothes and had hallucinations. He had lived in institutions for almost thirty years; he became occasionally excited, shouted the same words and was constantly indifferent. There were no significant physical signs.

Toluidine blue preparations showed mild irregularity in the architectural arrangement of the ganglion cells, many of the cells being vacuolated and clumped and surrounded by numerous glia cells (moderate neuronophagia). The cytoplasmic astrocytes were increased in number and size; the oligodendrocytes were only slightly more numerous. Fat was present in ganglion cells and occasionally in the glia. Slight proliferation of the capillary endothelium was observable. The lymph spaces of the vessel walls harbored a few free fat-laden cells. A few fat droplets in areas of unevenly stained myelin sheaths suggested slight degeneration of these structures. This patient, although the oldest of the 11 patients studied, showed no arteriosclerotic or presenile changes.

Case 9.—A woman aged 37 had the first psychotic symptoms at the age of 21 years. For the preceding four years she had been in an institution for the feeble-minded. She became disoriented, talked to herself and showed many catatonic features. The results of physical examination were essentially without significance. Periods of anxiety and excitement alternated with quiet, manneristic behavior; finally she became completely out of contact. The diagnosis was mental deficiency with psychosis, possibly schizophrenia.

Toluidine blue stains showed some neuron cells with deeply stained cell bodies and processes among the normal ones. Several pyramidal cells appeared shrunken; between them lay cell shadows. The cytoplasmic and fibrous astrocytes showed proliferative activity. Fat droplets were demonstrable in a few neuron cells but rarely in the glia. There was pronounced infiltration of vessel walls with fat, and fat-laden cells were observed in the adventitial spaces. The oligodendrocytic and microglial elements showed no essential changes.

Case 10.—A woman aged 33 had attempted suicide at the ages of 17 and 18 years because of ideas of persecution; she grimaced, had attacks of excitability and exhibited negativism. She was brought to the institution shrieking that she was being murdered. She paid no attention to her personal appearance and stared into space, under the influence of delusions and hallucinations. During her years in the institution she was destructive and aggressive. The results of physical examination were essentially without significance.

The toluidine blue stain showed many vacuolated ganglion cells and clumped Nissl bodies in the large pyramidal cells. The glia showed slight hypertrophy and pyknosis. Deposits of fat were seen in the ganglion cells and to a conspicuous degree in the vessel walls. The endothelial cells were swollen, and some pigment lay around the vessels.

Case 11.—A woman aged 36 had been psychotic since the age of 19. She read the Bible excessively, neglected her appearance, was under the influence of persecutory delusions, became excited and refused food through fear of being poisoned. She had auditory and visual hallucinations, talked incoherently and at times became aggressive. There were no significant physical signs.

The cortical structure was normal. There were no essential changes in the ganglion cells. The protoplasmic astrocytes showed only moderate increase in number and size; the fibrous astrocytes were slightly more numerous. The oligodendrocytes were unaltered. Stains for fat were not made. Myelin sheath stains revealed no pathologic conditions.

metrazol treatments, without benefit. The stream of thought remained rambling and irrelevant. Emotional response was flat and dissociated. There were momentary flashes of anxiety and aggressiveness.

Cresyl violet stains showed the pia to be slightly thickened. A large number of the ganglion cells were swollen, and a few were shrunken, with the dendrites

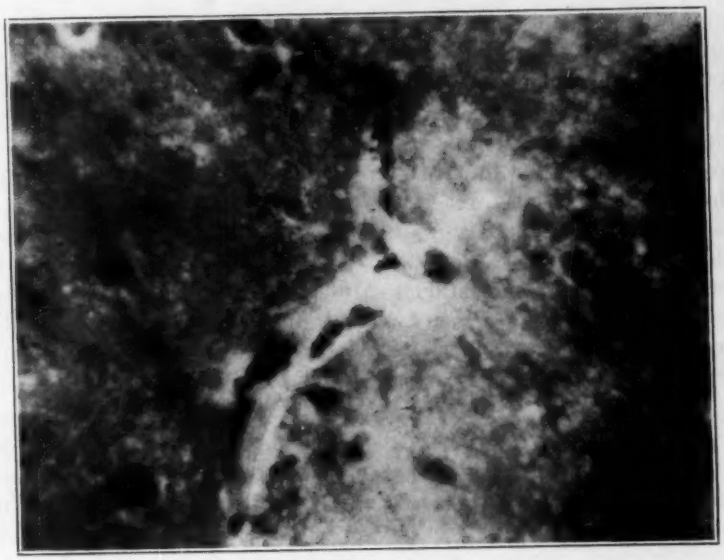

Fig. 4 (case 7).—Lipid deposits in the endothelial cells of arterioles of the brain (sudan III–hematoxylin stain; frozen sections).

Fig. 5 (case 12).—Increase in size and number of astrocytes, attached to a small artery, in a patient who had received insulin and metrazol shock therapy three years prior to frontal lobotomy (Cajal stain).

Case 12.—A woman aged 26 had the onset of mental illness at the age of 20; she refused to eat and to see friends and stayed in bed for six weeks. Suddenly she began to cry, demanded a priest, said she saw heaven and heard voices. There were no significant physical signs. She received a full course of insulin and

visible over a considerable distance. Proliferation of the cytoplasmic and the fibrous glia cells became particularly evident in Cajal preparations. Fat was present in both ganglion and glia cells, as well as in some arteriolar cells. The myelin pattern remained unchanged.

The histologic data in the cases are summarized in table 2.

It is difficult to correlate the time factor with the occurrence of the various pathologic changes; neither do the changes in the ganglion cells permit a distinct division into acute and chronic cellular disease. The loss of ganglion cells may be regarded as indicative of permanent change in the cortical architecture, whereas the alterations in the neuron cells noted in the first column of table 2 may possibly be transitory and reversible. A pronounced or extreme production of the astrocytic fibers is likely to be a lasting product of the action of a damaging agent. Similarly, reactions of cytoplasmic glia cells are considered signs of activity of the underlying process. The appearance of fat products and their transportation to the vessels deserve special discussion in connection with the primary influence of ether anesthesia on the brains of human beings and experimental animals.

TABLE 2.—*Histologic Data on the Brains of Eleven Patients with Schizophrenia Who Underwent Lobotomy*

	Histologic Changes						
	Ganglion Cells		Macroglia			Lipid Material in	
Case No.	Changes	Dropping Out	Cytoplasmic	Fibrous	Oligodendroglia	Glia	Vessels
2	+	—	+	++	—	+	+
3	++	—	+	+	—	+	++
4	(+)	+	+	..	—	—	(+)
5	++	—	++	+	(+)	—	—
6	+	—	+	+	—	+	++
7	..	—	+	—	..	+	+
8	+	(+)	++	+	+	+	++
9	+	—	+	+	—	(+)	+
10	+	—	(+)	—	+	—	+
11	—	—	(+)	..	(+)	—	—
12	(+)	—	(+)	++	..	..	(+)

In this table, .. indicates that no examination was made; — means that no changes were discovered; (+) denotes slight alteration, and +, pronounced changes.

COMMENT

Biopsies on the brains of schizophrenic patients were performed on a large scale by Elvidge and Reed.[2] Their studies, however, were confined to the white matter, particularly to the oligodendroglia, since their technic of aspirating brain substance from the parieto-occipital region through a needle with a Luer syringe did not provide sufficient cortical tissue.

With Hortega's silver impregnation method these investigators observed swelling and nuclear pyknosis of the oligodendrocytes in schizophrenic, in manic-depressive and in epileptic patients and concluded that the oligodendrocytes of the white matter are "sensitive indicators" of toxic products.

It is unfortunate that our material did not allow examination of the deep medullary layers of the white matter, where Elvidge and Reed almost exclusively noted the pathologic changes, since sufficient white matter was rarely obtained in our specimens. In 2 instances, however, it was possible to see in Hortega stains vacuolation of oligodendrocytes in the white matter.

Of the 11 patients, in only 1 (case 11) were merely negligible changes apparent, whereas in all the others pathologic alterations in the neurons, glia cells or vascular apparatus were disclosed.

The infiltration of fat and the transport of lipid products suggested of course the possibility that the ether narcosis may have been the sole, or a partial, factor responsible for these features, an observation raising the question of their relation to the underlying psychotic process independent of the influence of the ether anesthesia. In several biopsies (cases 3, 6, 7, 8 and 9) isolated cells laden with fat were noted in the adventitial spaces of small arteries and arterioles. Furthermore, fat had infiltrated the cells of the vessel walls and, to a lesser degree, had invaded the nerve parenchyma in the other cases.

From our control material, however, we assume that the ether narcosis could not have been primarily responsible for the presence of fat substances in our biopsy material, for the following reasons: 1. Examinations of the brains of 2 young nonschizophrenic patients who had died during abdominal operations performed with ether narcosis did not show infiltration of fat. 2. Changes in fat distribution were discovered in the brain in case 2, in which operation was done with anesthesia induced by local and intravenous administration of pentobarbital sodium. 3. Mueller [3] demonstrated in animals which were submitted to prolonged and frequently repeated ether narcosis infiltration of fat in ganglion cells and collection of fat both within and around the vessel walls. Weimann [4] reported the occurrence

2. Elvidge, A. R., and Reed, G. E.: Biopsy Studies of Cerebral Pathologic Changes in Schizophrenia and Manic-Depressive Psychosis, Arch. Neurol. & Psychiat. **40**:227 (Aug.) 1938.

3. Mueller, B.: Ueber Fettmetamorphose in den inneren parenchymatösen lebenswichtigen Organen nach einfachen und Mischnarkosen, Arch. f. klin. Chir. **75**:896, 1904-1905.

4. Weimann, W.: Exogene Intoxicationen, in Bumke, O: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1929, vol. 2, p. 58.

of increased fat products in the central nervous system in cases of ether intoxication but, unfortunately, omitted a detailed description. Elvidge and Reed,[2] confronted with the same question of the possible influence of ether on the central nervous system in their 19 cases (the majority of the operations had been performed with ether anesthesia), also made biopsies of brains of animals subjected to ether narcosis. Supported by negative results in these animals, they concluded that the changes they had described in human beings were not attributable to the influence of the ether.

When, in our animal experiments, rats were held under ether narcosis for two hours, biopsies of the brains failed to show any infiltration of fat; in the brains of cats, however, fat droplets appeared in a few cells of the vessel walls after two hours, and the fat-laden elements became more conspicuous with continuation of the ether narcosis. Few free cells were noted in the adventitial lymph spaces, and only occasionally were tiny clusters of isolated fat droplets observed. In all our animals the ganglion and glia cells remained free of lipid substances after a single ether narcosis lasting as long as four to six hours.

In order to determine unreservedly the significance of the presence of these lipid products, one must be aware that they are occasionally observed in the brains of apparently healthy young persons. Therefore, only massive infiltration and transport of fat can be considered pathologic.

The comparative frequency of the fat products seen in the various elements of the nerve tissue of our patients appears essentially to corroborate the observations of Cotton [5] and Josephy.[6] Freeman [7] described large deposits of lipids, both free and collected in phagocytic cells, in the basal ganglia of a 43 year old patient with catatonia who died of suffocation. This author summarized his study thus:

> . . . It may be concluded that in the brains of schizophrenic patients intercellular fat is more abundant than in the brains of normal individuals and also appears precociously.

Increase in the number and size of the protoplasmic and fibrous glia cells was rather constant. The especially severe disturbance of the fibrous glia in cases 2, 5 and 12, however, must, in the light of the investigations by Liebert and Weil,[8] be ascribed to the fact that the patients had at one time received metrazol or insulin shock or both forms of therapy.

Evaluation of the changes in the ganglion cells in our material had to be made with the utmost care, in view of the fact that slight swelling and shrinkage of the neurons might be attributed either to the fixation fluid or the staining methods. Spielmeyer warned against overestimation of rarefaction, dropping out of ganglion cells and presence of cell shadows, particularly when the glia appears inactive. On the other hand, numerous careful studies on schizophrenia have revealed notable changes in the neuron cells, comparable to ours, and not explainable on the basis of artefacts. Alzheimer,[9] Ranke [10] and Rosenthal [11] observed diffuse degeneration of ganglion cells, many of them swollen and filled with fat substances and others sclerotic. Cotton [5] demonstrated the frequent occurrence of lipid products in neuron cells. Josephy's [6] studies emphasized vacuolar and lipid degeneration and areas of paling and degeneration of individual neuron cells in distinct layers of the cortical substance, predominantly in the frontal areas. Localization of changes, especially in the frontal lobe, was observed by Goldstein,[12] Zingerle [13] and Hassin.[14] It should be stated that these various authorities expressed the common agreement that the changes bore no specific character but that,

5. Cotton, H.: Fatty Degeneration of the Cerebral Cortex in the Psychoses with Special Reference to Dementia Praecox, J. Exper. Med. **22**:492, 1915.

6. Josephy, H.: Beiträge zur Histopathologie der Dementia Praecox, Ztschr. f. d. ges. Neurol. u. Psychiat. **86**:391, 1923.

7. Freeman, W.: Lipoid Degeneration Products in the Thalamus and Globus Pallidus in Schizophrenia, A. Research Nerv. & Ment. Dis., Proc. **5**:378, 1928.

8. Liebert, E., and Weil, A.: Histopathologic Changes in the Brain Following Experimental Injections of Metrazol, Arch. Neurol. & Psychiat. **42**:690 (Oct.) 1939.

9. Alzheimer, A.: Beiträge zur pathologishen Anatomie der Dementia praecox, Psychiat.-Neurol. Wchnschr., 1913, p. 301; Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:621, 1913.

10. Ranke, O.: Katatonie mit Hirnschwellung, in Nissl, F.: Beiträge zur Frage nach der Beziehung zwischen klinischen Verlauf und anatomischen Befund bei Nerven- und Geisteskrankheiten, Leipzig, 1913, vol. 1.

11. Rosenthal, S.: Katatonie mit Hirnschwellung, in Nissl, F.: Beiträge zur Frage nach der Beziehung zwischen klinischen Verauf und anatomischen Befund bei Nerven- und Geisteskrankheiten, Leipzig, 1913, vol. 1.

12. Goldstein, K.: Zur pathologischen Anatomie der Dementia Praecox, Monatschr. f. Psychiat. u. Neurol. **25**:565, 1909.

13. Zingerle, O.: Zur pathologischen Anatomie der Dementia Praecox, Monatschr. f. Psychiat. u. Neurol. **27**:285, 1910.

14. Hassin, G. B.: The Present Status of the Histopathology of Dementia Praecox, Dementia Praecox Stud. **1**:7, 1918; Histopathology of the Peripheral and Central Nervous System, ed. 2, New York, Paul B. Hoeber, Inc., 1940.

nevertheless, they must be regarded as the substrate of the psychosis. It appears erroneous to dismiss the observations noted as insignificant—an attitude preferred by Dunlap [15] and Peters.[16]

Schizophrenia is a clinical concept and cannot be considered as a unified disease. It is not at all surprising, therefore, that we found among our "typically schizophrenic" patients at least 2 presenting unequivocal organic disease of the brain (cases 1 and 3), in accordance with the experiences of Ferraro,[17] Malamud and Boyd [18] and others. Ferraro [17] stated the belief that the organic changes in the brains of schizophrenic patients are compatible with the diagnosis of schizophrenia. In certain cases he related the structural damage to functional changes, which he interpreted as complicating, not causative, factors of the psychosis.

The problem remains whether the changes observed are the cause of the psychosis, whether they are a consequence thereof or whether they are mere lateral effects of other factors influencing the central nervous system, without direct relation to the psychosis. Suffice it to say, they resemble changes frequently observed in association with chronic infections and metabolic disturbances.[19]

SUMMARY

Histologic examination of biopsy specimens from the prefrontal cortex of patients with chronic schizophrenia revealed degenerative changes of the ganglion cells and progressive and regressive reactions of the glia and blood vessels, such as are commonly seen in cases of chronic intoxications and metabolic disorders. Study of control material obtained from nonschizophrenic human beings and experimental animals proved that the changes were not attributable to the ether narcosis during which the material had been obtained.

15. Dunlap, C. B.: The Pathology of the Brain in Schizophrenia, A. Research Nerv. & Ment. Dis., Proc. **5**:371, 1928.

16. Peters, G.: Zur Frage der pathologischen Anatomie der Schizophrenie, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:361, 1937.

17. Ferraro, A.: Recent Views and Leading Points on the Toxic Approach to Mental Disease, Psychiatric Quart. **5**:625, 1931; Significance of Pathological Changes in the Brain of a Case Clinically Diagnosed Dementia Praecox, J. Neuropath. & Exper. Neurol. **2**:84, 1943; **1**:188, 1942; Histopathological Findings in Two Cases Clinically Diagnosed Dementia Praecox, Am. J. Psychiat. **13**:883, 1943.

18. Malamud, N., and Boyd, D. A.: Sudden Brain Death in Schizophrenia with Extreme Lesions in Cerebral Cortex, Univ. Hosp. Bull., Ann Arbor **4**:33, 1938.

19. Kirschbaum, W. R.: Ueber den Einfluss schwerer Leberschädigungen auf das Zentralnervensystem: I. Gehirnbefunde bei akuter gelber Leberatrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **77**:536, 1922. Hassin.[14] Ferraro.[17] Weimann.[4]

RELATION OF NARCOLEPSY TO THE EPILEPSIES

A CLINICAL-ELECTROENCEPHALOGRAPHIC STUDY

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In Wilson's [1] classic discussion of the narcolepsies strong evidence is produced to justify their inclusion in the family of the epilepsies. Adie [2] earlier postulated, on the basis of his clinical observations, that narcolepsy is a disease entity. In recent years electroencephalography, which has proved to be of much value in the study of the epilepsies, has been focused on the problem of narcolepsy in an attempt to resolve the impassé resulting from these two clinical schools of thought.

Electroencephalographic observations [3] are unanimous as to the occurrence of various stages of "sleep waves" during the sleep component of the narcoleptic seizure. In early sleep, whether physiologic or narcoleptic, the characteristic electroencephalographic pattern is of the low amplitude, high frequency (18 to 25 waves per second) type; as sleep progresses slow wave discharges dominate the record. In deeper sleep 14 per second discharges are recognized as a transient phenomenon.[4] Blake and her associates [3c] have expressed the opinion that the chief distinguishing feature between normal and narcoleptic sleep is the precipitous onset of the latter. Dynes and Finley,[3a] on the basis of a series of 22 cases, arrived at the conclusion that the "spontaneous" interseizure electroencephalograms of morbid sleepers (narcoleptic patients) show no characteristic similarities to the wave patterns associated with the epilepsies.

In the present communication a detailed clinical and electroencephalographic study of 10 cases of a severe disturbance of sleep function is presented. The disorder manifested itself in paroxysmal, diurnal, entirely inappropriate and uncontrollable sleep. In 5 cases affective stimuli induced cataplectic muscular phenomena. In this series of cases inconstant, but definite, abnormalities of the electroencephalogram were observed in the waking state. Moreover, these abnormalities were qualitatively similar to, but quantitatively less prominent than, the electroencephalographic changes commonly associated with the epilepsies.

REPORT OF CASES

CASE 1.—*History.*—B. J. S., a Negro aged 23, had had a formal fifth grade education, but his acquired learning was far above this level. He was unable to carry out his duties as a soldier on account of irresistible attacks of sleep.

Mild seizures of sleep first occurred in 1927, at the age of 8 years. At the age of 9 years he sustained a fracture in the left parietal region of the skull. At this time the intensity of the narcoleptic spells became accentuated. Attacks of sleep occurred from three to five times a day. For the last fourteen years there had been no increase in frequency or intensity of the attacks. The patient stated that sleep was ushered in by "a sort of curtain coming over" his eyes. He said that after the sleep state he felt weak for several minutes. Numerous automobile accidents had occurred as a result of his inability to keep awake, even while driving. Nocturnal sleep was not impaired. There was no evidence of cataplectic phenomena.

He stated that he had had only the ordinary diseases of childhood. He denied having had any serious illness other than the attacks of sleepiness. He said that 1 sister, at the age of 14 years, began to have narcoleptic attacks of even greater severity than his own. One brother was said to have had "spasms," which later disappeared. Ten other siblings were all presumably normal. A maternal aunt had narcoleptic seizures beginning at the age of 20 years. She "slept almost all the time." She died at the age of 40, while "asleep."

Examination.—The patient was well developed and lightly pigmented. He stuttered somewhat during ordinary conversation. Occasionally he showed an involuntary, mild, coarse tremor of the body. The muscles

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This work was aided in part by a grant from the Supreme Council, Thirty-Third Degree Scottish Rite, Masons of the Northern Jurisdiction, U. S. A.

1. Wilson, S. A. K.: The Narcolepsies, Brain **51**: 63-109, 1928.

2. Adie, W. J.: Idiopathic Narcolepsy: A Disease Sui Generis, with Remarks on the Mechanism of Sleep, Brain **49**:257-306, 1926.

3. (*a*) Dynes, J. B., and Finley, K. H.: The Electroencephalograph as an Aid in the Study of Narcolepsy, Arch. Neurol. & Psychiat. **46**:598-612 (Oct.) 1941. (*b*) Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, ibid. **34**:1133-1148 (Dec.) 1935. (*c*) Blake, H.; Gerard, R. W., and Kleitman, N.: Factors Influencing Brain Potentials During Sleep, J. Neurophysiol. **2**:48-60, 1939.

4. Davis, H.; Davis, P. A.; Loomis, A. L.; Harvey, E. N., and Hobart, G. A.: Human Brain Potentials During the Onset of Sleep, J. Neurophysiol. **1**:24-38, 1938.

of the iris contracted slowly to light and in convergence. General perception of sensory stimuli and motor function seemed unimpaired. No pathologic reflex pattern was elicited. Ophthalmoscopic study showed moderate entwining of the retinal arteries and veins, most pronounced on the left side. The basal metabolic rate measured — 23 per cent on Feb. 12, 1942 and — 40 per cent on February 16. The Wassermann reaction of the blood was negative.

Electroencephalographic Studies.—Repeated electroencephalographic studies showed dominant alpha sequences,

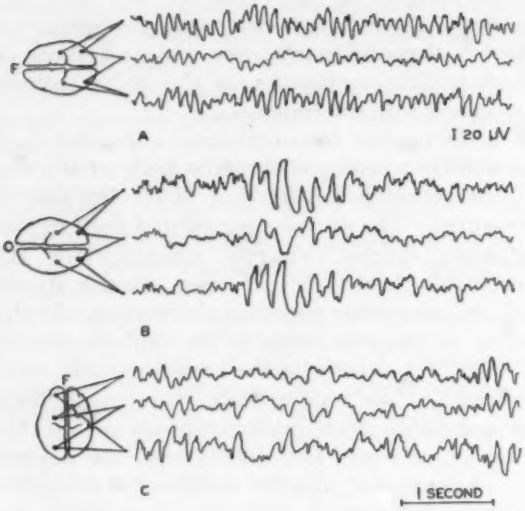

Fig. 1 (case 1).—*A*, basic pattern when the patient was awake; *B*, burst of low frequency activity, unassociated with sleep or movement; *C*, waves appearing during early sleep.

the frequencies ranging from 8.5 to 10 per second (fig. 1 *A*). Short bursts of waves of lower frequency (approximately 6 per second) were observed in the frontal leads. These volleys were unassociated with any recognizable motor activity or evidence of sleep (fig. 1 *B*). During the recording, for approximately a two minute interval, breathing became audible, and volitional response to auditory stimuli was no longer elicited. The electroencephalogram (fig. 1 *C*) associated with this "sleep" state appeared similar to that obtained in early normal sleep. Hyperventilation for two minutes resulted in a moderate increase in the low frequency component of the basic "awake" type of electroencephalogram.

Case 2.—*History.*—C. McL., a white man aged 25, reported at "sick call" when he became worried lest he fall asleep on guard duty and be court-martialed.

As well as he was able to ascertain, he had had spells of sleepiness ever since he was born. The attacks were not preceded by an aura. The seizures occurred two to six times a day. He had been arrested for speeding and passing red traffic lights during these spells. On awakening from an attack he felt well and was able to resume whatever task he was performing at the time. There had been little variation in the pattern, intensity or frequency of the seizures. They were uninfluenced by any medication. Any strong excitement made him "weak in the knees." Nocturnal sleep was undisturbed except for occasional "nightmares."

He stated that at the age of 2 years he had "milk poisoning" and nearly died. This illness left him "nervous" and with a tendency to stutter. This disturbance was more noticeable during periods of tension. In addition to the ordinary diseases of childhood and an attack of diphtheria, he had influenza in 1935.

The patient was an only child. There was no history of narcolepsy in the family. The mother was an invalid; she had had one or two "nervous breakdowns" and had been operated on for the relief of hyperthyroidism. Two maternal aunts also suffered from hyperthyroidism.

Examination.—The patient was short, moderately stout and blond. He appeared serious and intelligent. Aside from stuttering, paralysis of the right pharyngopalatine muscle and brisk, but equal, deep tendon reflexes on the two sides, no important abnormalities at the gross neurologic level were elicited. The temperature ranged around 97.5 F., and the pulse rate averaged 65 beats per minute. Several determinations of the basal metabolic rate showed only moderate decrease in the utilization of oxygen. The cholesterol content of the blood was 0.182 mg. per hundred cubic centimeters and the dextrose tolerance curve showed only a slight central elevation.

Electroencephalographic Study.—The electroencephalograms were characterized by a dominant alpha pattern. The voltage was relatively high, but well modulated. There was a well regulated frequency of approximately 10 waves per second (fig. 2 *A*). Occasional bursts of 6 per second waves arose in the midst of prominent alpha activity (fig. 2 *C*). Narcoleptic spells during the recordings were associated with waves of the type usually seen during physiologic sleep. Auditory stimuli (impact of metal rods) during the narcoleptic seizures brought out excellent volleys of alpha waves (fig. 2 *B*). Hyperventilation induced no gross change in the electroencephalogram.

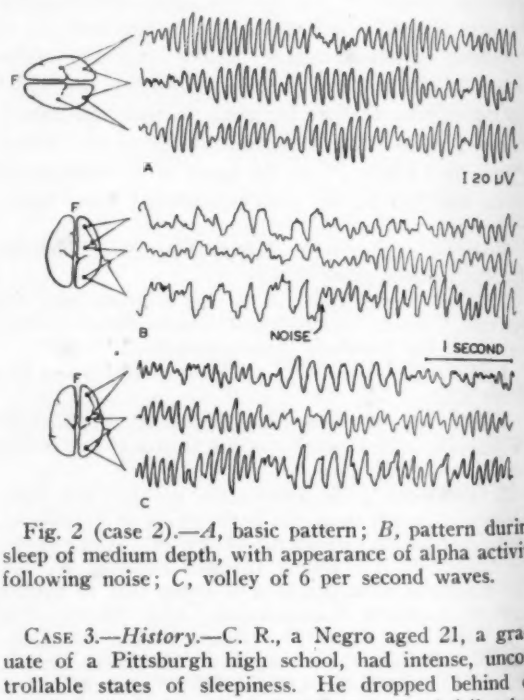

Fig. 2 (case 2).—*A*, basic pattern; *B*, pattern during sleep of medium depth, with appearance of alpha activity following noise; *C*, volley of 6 per second waves.

Case 3.—*History.*—C. R., a Negro aged 21, a graduate of a Pittsburgh high school, had intense, uncontrollable states of sleepiness. He dropped behind on marches, slept at meals and at lectures and fell asleep whenever he was left alone.

Attacks, which were first noted at the age of 3 or 4 years, were preceded by a mild headache. The cephalalgia became more intense if he could not sleep.

A typical instance of the patient's general behavior may be obtained from his boxing activity. While waiting to box, he would fall asleep; then he would "whale the devil" out of his opponent and five minutes later was again asleep. Nocturnal sleep was not disturbed. Emotional excitement made him "weak all over" and produced "a heavy feeling in the stomach."

He was struck in the left eye with a baseball bat in 1938; since then he had had ptosis of the left eyelid. He stated that drooping of the lid was more obvious when he was tired or at the end of the day. He had

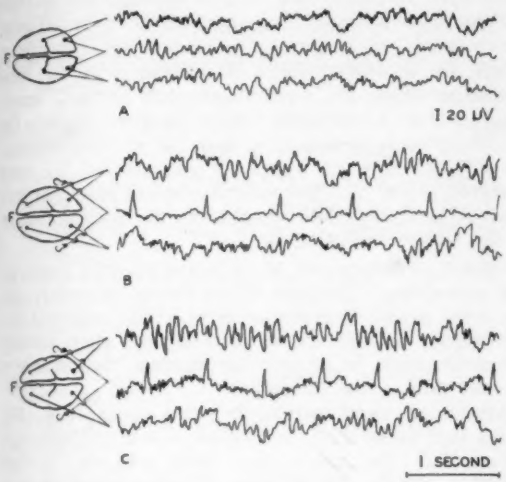

Fig. 3 (case 3).—*A*, basic pattern; *B*, pattern before hyperventilation; *C*, pattern after one and a half minutes of hyperventilation.

had the ordinary diseases of childhood. He denied having had influenza or grip.

He stated that 1 sister had an abnormal tendency to sleep but that her attacks were not as severe as his own. His mother had spells of dizziness, "from high blood pressure," but she did not "fall out."

Examination.—The patient was rather tall and thin and appeared intelligent. He talked well and appropriately. There was pronounced ptosis of the left eyelid. Enopthalmos was not observed. The pupils were round and equal and measured about 2.5 mm. in diameter. The muscles of the iris reacted well to light and in accommodation. On lateral gaze nystagmoid jerks were observed. No evidence of dysfunction of the perception of sensory stimuli was elicited. Deep tendon reflexes were active and equal on the two sides. No gross motor dysfunction was recognized.

Electroencephalographic Study.—The electroencephalograms showed a random, high frequency discharge of low amplitude (fig. 3*A* and *B*). Occasional oscillations of long duration were observed; these had distorted, square wave characteristics (not shown in the figure). No narcoleptic seizures were manifest during the tests. Hyperventilation evoked sequences of rhythmic oscillations approximately thirty seconds after the onset of overbreathing. This rhythmicity became strongly dominant after about two minutes of hyperventilation (fig. 3*C*). The R spike of the electrocardiogram was a prominent characteristic of the records from the biaural leads.

Case 4.—*History.*—C. L. M., a Negro aged 22, began school at the age of 8 years; by the age of 17 years he had progressed to the fourth grade. He was relieved of army field duty because of his inability to stay awake and was then assigned to duty as a furnace fireman. Here he had to be constantly watched for fear that he would sleep on the furnaces and injure himself.

From his statements it was apparent that he had suffered from a sleep disorder all his life. He estimated that he slept eighteen hours a day. He stated that the onset of sleep was not accompanied by any aura. The intensity of the narcoleptic disturbance remained practically constant. He was said often to show violent outbursts of temper when he was awakened. When he became emotionally excited, he fell to the floor but did not lose consciousness.

He had whooping cough at the age of 7 years and measles at the age of 14 years, at which age he struck his head while swimming and was knocked unconscious. Since then he had had headaches most of the time. At the age of 18 he had an attack of pneumonia. He denied having had influenza or grip.

He stated that all his brothers were hot tempered. One brother (aged 14 years) spent most of his time in bed sleeping; essentially he got up only to eat. A younger sister had "convulsions."

Examination.—One was immediately attracted by the continuous, shy, faint smile on the patient's face. He was tall and not darkly pigmented. In view of the subject's limited education and general sleepiness, his conversation was good. His answers to queries were often delayed (he said he was hard of hearing), but they were always appropriate. Jerking of the head and body was observed, the movements being random and of small amplitude. The nuchal flexure was almost absent. The face showed some static asymmetry. The left side of the face was flattened. Dynamic (volitional and

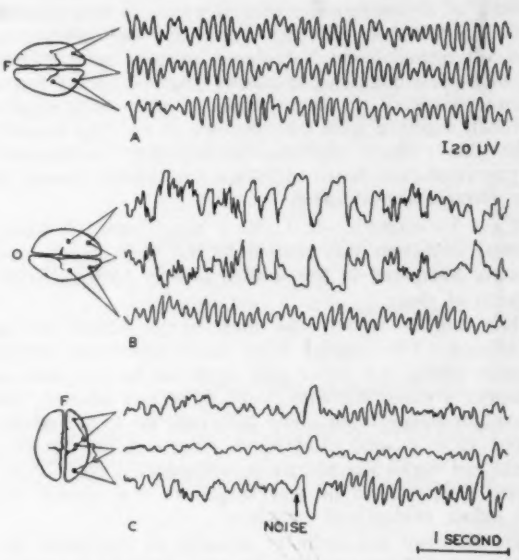

Fig. 4 (case 4).—*A*, basic pattern; *B*, abnormal wave forms in the left frontal lead; *C*, waves appearing during sleep, with response to an auditory stimulus.

emotional) motor function of the facial muscles appeared intact. The patient was able to hear a watch tick at a distance of over 30 cm. with the right ear and at a distance of only 5 cm. with the left ear. In each ear bone conduction was more acute than air conduction. There was moderate reduction in volume of the muscles of the left upper extremity. The biceps region had a circumference of 22.5 cm. on the right side and of 21 cm. on the left side. The hand grip was equally dimin-

ished on the two sides. The finger to nose test, with the eyelids closed, showed some decomposition of movement and inaccuracy of placement on both sides. Sensory perception to pinprick, light touch and vibration did not appear grossly disturbed. Stereognostic function seemed intact. Deep tendon reflexes were active and approximately equal on the two sides. No pathologic reflexes were elicited. Clonic phenomena were not observed. Stereoscopic roentgenograms of the head showed no gross abnormality. The Kahn reaction of the blood was negative.

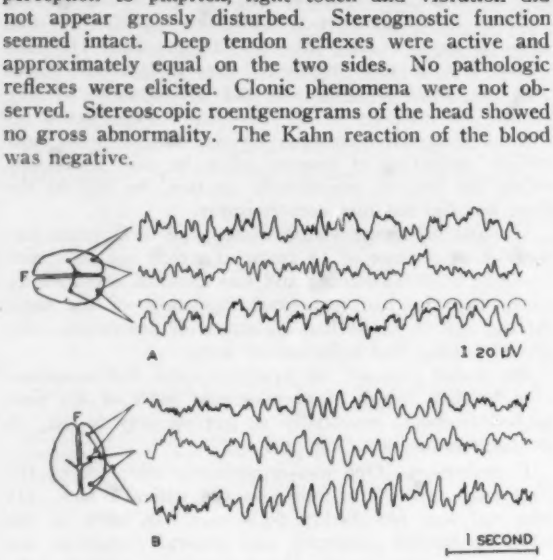

Fig. 5 (case 5).—*A*, basic pattern, with predominantly low frequency discharges; *B*, burst of slow waves.

Electroencephalographic Examination.—There was a dominant alpha frequency of approximately 10 waves per second (fig. 4 *A*). A transient abnormality, consisting of asymmetrically peaked waves of large amplitude and variable frequency (fig. 4 *B*), was observed in the left frontal lead. Narcoleptic seizures were evident in each recording. In one tracing (fig. 4 *C*) wave forms characteristic of the early stages of sleep were clearly evident, together with the influence of auditory stimuli. The "on" effect of the stimulus was pronounced. Hyperventilation failed to induce any notable change in the electroencephalogram.

CASE 5.—*History.*—R. L. R., a Negro aged 19, whose formal education was limited to the tenth grade, was greatly hampered in his service activity by irresistible attacks of sleep.

His mother stated that these spells began during childhood. The attacks were more numerous during fatigue states, but under any condition he had several seizures a day. No history of aura was elicited; he "just got sleepy." As a boy he would go to a "movie" about 10 a. m. and often leave after 4 p. m., but still could not recall the picture in a connected way. Nocturnal sleep was in no way disturbed. Excitement did not induce evidence of cataplexy.

He had had the ordinary diseases of childhood, including diphtheria. In 1941 he was treated for gonorrhea and a lesion of the penis, which he stated was not due to syphilis. At times he drank alcohol to excess. He denied having had influenza or grip.

His mother was apparently addicted to the use of alcohol. The father was said to be a "constitutional psychopath." It was stated that a maternal first cousin, aged 44, was narcoleptic and that a maternal aunt had been institutionalized for a mental disorder.

Examination.—The patient was tall, heavy and darkly pigmented. He talked well and appropriately. He readily comprehended and responded well to fairly complex questions. The pupils were round and equal and measured about 1.5 mm. in diameter. The muscles of the iris reacted to light and in accommodation. There was ptosis of the right eyelid. With increased intensity of illumination in the left eye the ptotic lid closed reflexly. Sensory and motor function showed no gross general or local impairment except that already noted. Deep tendon reflexes were active and equal on the two sides. Abadie's sign was present bilaterally.

Electroencephalographic Study.—Figure 5 *A* shows the pattern characteristic of the waking state obtained from bipolar parieto-occipital leads. The main deflections have durations close to two hundred milliseconds (5 waves per second). Superimposed is faster activity, which tends to obscure the fundamental frequency. There are occasional shifts of dominance of the slow discharges from the right to the left cerebral hemisphere. For a relatively short interval during the recording many sequences of fast (20 to 22 waves per second) and slow (6 waves per second) activity were observed (fig. 5 *B*). The subject was not asleep at this time. Hyperventilation brought out no marked change in the electroencephalogram.

CASE 6.—*History.*—O. M., a Negro aged 35, appeared dull and sleepy. The limit of his formal education was the third grade of grammar school. He reported his narcoleptic disorder almost immediately after joining the army, when he became apprehensive that it might get him into serious difficulties.

Attacks of sleep were first noted about 1930. He stated that about 1925 he had an attack of "influenza pneumonia." He had a high fever and was in bed almost a month. At the time of examination he had two to six narcoleptic attacks daily, each lasting about

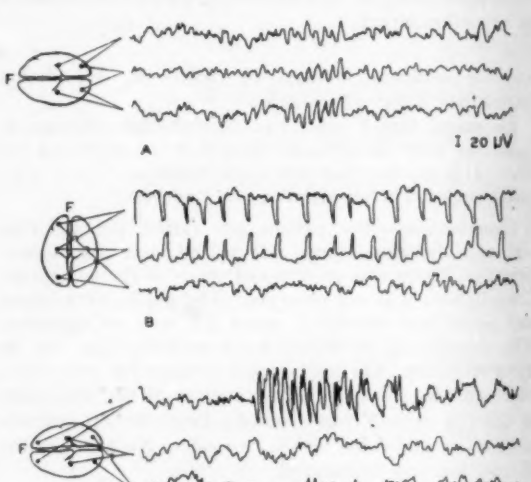

Fig. 6 (case 6).—*A*, basic pattern; *B*, psychomotor discharge in the left parietal lead; *C*, abnormal wave forms in a later record.

five minutes. He would fall asleep under almost any circumstance—at drill, at meals or at the movies. Each spell came on with an overpowering desire to sleep that he could not fight off. He denied having any cataplectic episodes during excitement. He often walked in his sleep.

The early medical history was vague, but one gathered that he had had most of the diseases common to childhood. Aside from the "influenza pneumonia" and

accidental trauma to the left leg, he appeared to have been in good health.

The family history was noncontributory; actually, he was vague and uncommunicative with respect to it. He stated he had a child 12 years old, who was well.

Examination.—The patient was tall, thin and darkly pigmented. No pronounced deviation from the normal was evident. He talked slowly but well. No abnormal sweating or greasiness of the skin was observed. There was no increase in salivation. The pupils were approximately 3 mm. in diameter and were equal. The muscles

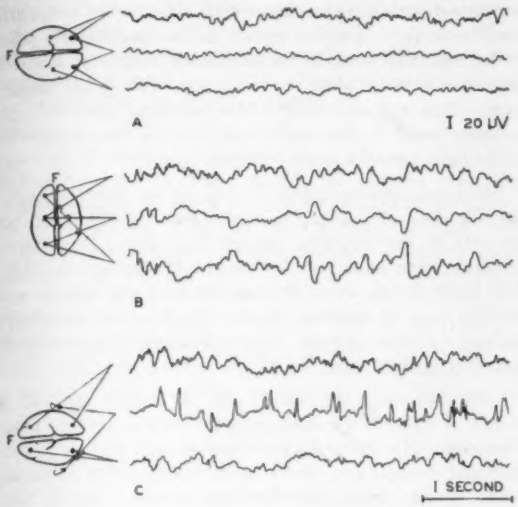

Fig. 7 (case 7).—*A*, basic pattern; *B*, waves appearing during sleep in a narcoleptic seizure; *C*, spike waves in the lead from the left ear.

of the iris reacted well to light and in convergence. Motor function appeared normal. Perception of sensory stimuli was diminished over the lateral aspect of the left leg. This extremity had been the site of spike and bullet wounds. Deep tendon reflexes were decreased in amplitude but were active and equal on the two sides. A dextrose tolerance test gave an entirely normal curve. The Kahn reaction of the blood was negative.

Electroencephalographic Study.—No narcoleptic spells were recognized in the electroencephalograms. Basically, the tracing revealed waves of low amplitude. The occipital leads showed only a moderate proportion of 10 per second waves (fig. 6*A*). In figure 6*B* is shown a burst of abnormal wave forms from the left parietal lead, which persisted for nearly three minutes. In figure 6*C* the abnormality appears in the frontal region in a record taken two days after the tracing in figure 6*B*. This abnormality consists of a volley of high voltage waves of one hundred milliseconds' duration, followed by oscillations with fundamental durations two to three times as long.

CASE 7.—*History.*—W. L. W., a Negro aged 27, had progressed in his formal education in an entirely normal manner to the second year of high school. He tried to conceal his uncontrollable tendency to sleep, but it was noted that whenever the order was given to stand "at ease" he fell asleep. This defect led to his hospitalization.

He stated that in 1928 he had an attack of "grip" and that since then he had had an ever progressive tendency to sleep. However, his mother stated that he had suffered from seizures of sleeping since childhood. She also said that before his attacks of sleep he "shook and worked his mouth." Nevertheless, during the past four or five years he had shown an almost cyclic recurrence of diurnal irresistible sleep states. He had on several occasions awakened to find that he had crossed busy city streets. This made him feel "shaky." His friends stated that during these states of sleep walking his eyelids were shut but he could carry on conversation. At night he often awakened from deep sleep and remained awake for one or two hours. Strong emotion made him "weak all over."

He had had the common diseases of childhood, but he did not have mumps until the age of 15 years. When he was 13 years old he had the aforementioned attack of "grip," and at the age of 16 he had rheumatism, which immobilized him for approximately one month.

Two siblings appeared entirely normal. Another brother, aged 21, had attacks of sleep like the patient's.

Examination.—The patient was of medium size, well developed and darkly pigmented. He talked slowly but well and appropriately. He walked with a slow but not abnormal gait. The head was round; the facial features were blunt. The pupils were round and equal and measured approximately 2 mm. in diameter. The muscles of the iris reacted well to light and in convergence. The cranial nerves appeared free from gross abnormality. No motor or sensory dysfunction was observed. The deep tendon and superficial reflexes were active and equal on the two sides. Abadie's sign was noted bilaterally, but Biernacki's sign was not present. Determination of the basal metabolic rate, the dextrose tolerance test and serologic examinations of the blood all gave normal results. Stereoscopic roentgenograms of the head revealed nothing abnormal.

Electroencephalographic Study.—The electroencephalogram was of the low amplitude, random frequency type. Occasional rhythmic sequences of about 17 waves

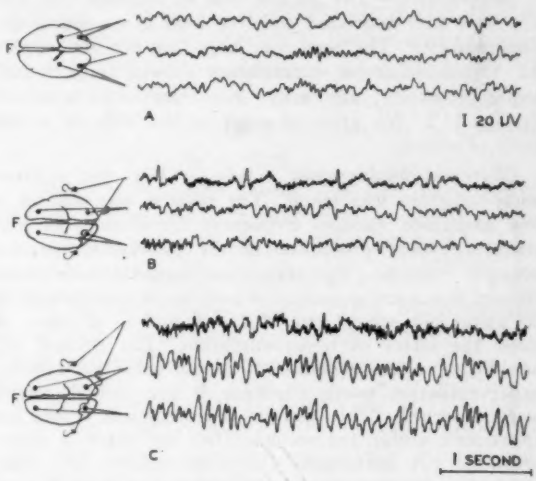

Fig. 8 (case 8).—*A*, basic pattern; *B*, pattern before hyperventilation; *C*, pattern during hyperventilation, with rhythmic fronto-occipital activity.

per second were observed (fig. 7*A*). During the narcoleptic state wave forms characteristic of normal sleep were recognized (fig. 7*B*). The left ear lead (middle line of figure 7*C*) showed random spike forms, which were in no way synchronous with the radial pulse.

CASE 8.—*History.*—C. T., a white man aged 25, was referred for electroencephalographic study by Dr. Antoine Schneider, Washington, D. C. The patient appeared intelligent. He said his life had been ruined

by "narcolepsy." At the age of 12 years he had "spinal meningitis," and for several months after the infection he was "cross eyed." In his fourth year of high school, at the age of 17, he began to have spells of sleepiness. These states had become progressively more intense, so that now he often awakened to find that he had traversed several busy streets. He greatly feared that this might result in a serious accident. However,

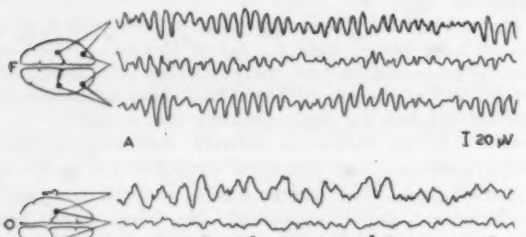

Fig. 9 (case 9).—*A*, basic pattern; *B*, during narcoleptic seizure; *C*, volley of slow waves during hyperventilation.

he was most depressed by his attacks of sleep while he was working. This condition had made it difficult for him to keep a position for any length of time.

Examination.—The patient was of medium size and appeared well nourished and free from gross neurologic abnormalities. The head was large, but not abnormally so. Ophthalmoscopic examination showed some retinal hypervascularity; the artery-vein ratio was approximately 1:1. No gross changes in the disk or retina were observed.

Electroencephalographic Study.—Only one electroencephalogram was taken. The pattern was that of a low amplitude, random frequency. Oscillations of low frequency were prominent in the symmetric parieto-occipital records. The transverse occipital derivations showed dominant sequences of activity of approximately 20 waves per second (fig. 8 *A*). *B* and *C* of figure 8 show the effect of hyperventilation. The control, *B*, has little or no evidence of alpha activity. During hyperventilation many rhythmic 9 per second waves were observed. This definite alpha pattern made its appearance within ten seconds after the onset of overbreathing. A maximum was soon reached and was roughly maintained during the entire period of hyperventilation (three minutes). Within a minute after the cessation of overbreathing the 9 per second waves were replaced by oscillations approximating the control type.

CASE 9.—*History.*—H. G., a Negro aged 18, born in Alabama, had completed the eighth grade of grammar school. He could not keep from sleeping; on the march he stumbled, and in the "at ease" position he immediately went to sleep. He stated that between the ages of 8 and 10 years he began to sleep at inappropriate times. At about the age of 15 these attacks of irresistible sleep occurred four to five times a day. From that time their intensity and frequency remained constant. Aside from an intense desire to sleep no aura was experienced. He denied any dystonic reaction to emotional stimuli. Nocturnal sleep was often interrupted by long intervals of insomnia.

He had had the common diseases of childhood, with no apparent sequelae. At the age of 16 years he had influenza.

He had 5 sisters and 1 brother, all of whom were said to be well. His father, a veteran of World War I, had left hemiplegia in early middle life. The nature of the disorder was not determined.

Examination.—The patient was well developed, well nourished and darkly pigmented. He had a singularly intelligent face. During conversation, particularly when he became animated, he manifested a hesitancy of speech that was closely akin to stuttering. No gross impairment of motor or sensory function was observed. All reflexes were active and equal on the two sides. No pathologic reflexes were elicited.

Electroencephalographic Study.—The electroencephalogram showed a beautiful alpha pattern (10 waves per second) in the occipital region (fig. 9 *A*). Narcoleptic seizures were observed during the recording (fig. 9 *B*). The wave forms were characteristic of the pattern seen during sleep of medium depth. During hyperventilation volleys of slow waves (approximately 6 per second) were recognized (fig. 9 *C*).

CASE 10.—*History.*—J. H. S., a Negro aged 35, a native of Pittsburgh, had received only a seventh grade education. His general conversation was mature in context and vocabulary. Because of his inability to remain awake it was impossible for him to carry out his military duties.

In September 1932 the patient weighed 165 pounds (74.8 Kg.); within three months he weighed 230 pounds

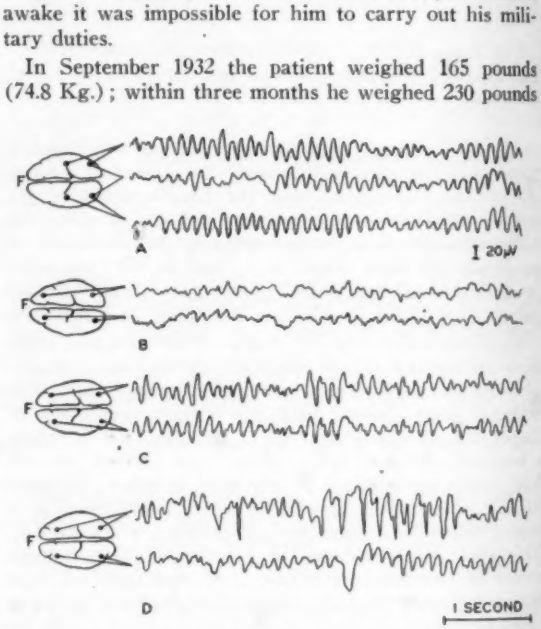

Fig. 10 (case 10).—*A*, basic pattern; *B*, waves appearing during early sleep, just before hyperventilation; *C*, pattern at the beginning of hyperventilation; *D*, abnormal waves during early hyperventilation.

(104.3 Kg.). During the interval of increasing weight he began to have dizzy spells, which continued up to the present. During such spells he stuttered and found it difficult to "think and say things." He did not lose consciousness at this time but became "weak all over." These attacks occurred two or three times a day.

After each seizure he slept. At times, however, sleep became irresistible, even without the prelude just described.

Aside from the ordinary diseases of childhood, he had influenza in 1923 and again in 1929.

He denied that any other member of his family had any nervous disturbance or sleep disorder. His family consisted only of average-sized persons.

Examination.—The patient was lightly pigmented, tall and obese. There was no definitely abnormal distribution of fat. He repeatedly fell asleep while being examined. No gross neurologic abnormality was elicited. The pupils were round and equal and measured about 3 mm. in diameter. The muscles of the iris contracted well to light and in convergence. There was no gross disturbance of the visual fields. No abnormal sweating or greasiness of the skin was seen.

Electroencephalographic Study.—It was difficult to obtain an electroencephalogram from this subject while he was awake. A short sample of record from the occipital region obtained in this state shows an excellent 9 to 10 waves per second (alpha) pattern (fig. 10 *A*). Waves characteristic of various depths of sleep dominate the record. Before hyperventilation, early sleep waves are seen (fig. 10 *B*). Almost immediately after the onset of hyperventilation sleep waves are replaced by prominent alpha sequences (fig. 10 *C*). During hyperventilation a short volley of approximately 5 per second, asymmetric waves is observed (fig. 10 *D*).

COMMENT

In 5 cases the classic syndrome of Gélineau (irresistible, inappropriate diurnal sleep and transient physical powerlessness under the influence of affective stimuli) was evident clinically. In the other 5 cases the isolated symptom of uncontrollable sleep was present.

An outstanding feature in this series of cases was the familial nature of the disorder. Five patients had a brother, a sister or a first cousin who was subject to a sleep disorder or to epilepsy. Two patients each had a sibling who was narcoleptic and a sibling who was epileptic. The strong familial characteristic observed in this series of cases is unique in the literature of narcolepsy.

Case 7, in which there was a history of a convulsive disorder in childhood, is similar to the case of Gowers, cited by Wilson.[1] Stuttering was a prominent characteristic in 3 cases. J. H. S. (case 10) stuttered as a prelude to the cataplectic component of his seizure pattern.

In 2 cases the onset of symptoms began after an attack of influenza. The latent periods from the infection to the appearance of the sleep disorder were three and five years respectively. In certain instances a head injury apparently acted as a catalytic agent to increase the intensity or frequency of the sleep seizures.

On gross neurologic examination scattered signs were recognized. In case 4 there was a strong possibility of trauma at birth. The presence of hypothalamic dysfunction was difficult to rule out in case 10.

The basic electroencephalograms, taken between intervals of "sleep," showed no wave pattern characteristic of the narcoleptic syndrome. The proportion of alpha frequencies varied from complete dominance to almost complete absence.

The abnormal wave forms observed in the majority of the records were similar, in all essentials, to those obtained from epileptic persons. The isolated bursts of high voltage, slow waves in the electroencephalograms of case 1 (fig. 1 *B*), case 2 (fig. 2), case 4 (fig. 4 *B*) and case 5 (fig. 5 *B*) all occurred within two to four minutes after the start of the recording. They were in no way associated with any clinical or electroencephalographic evidence of sleep. The record in case 6 (fig. 6) is an excellent example of the wave types encountered with certain of the epilepsies. The "epileptic" response to hyperventilation was noteworthy in case 9 (fig. 9 *C*) and in case 10 (fig. 10 *D*). Under the test conditions established, these responses were seldom seen in the absence of any gross change in the mechanisms or components of carbohydrate metabolism.[5] The establishment of a dominant rhythmic activity in a random frequency pattern during hyperventilation was observed in case 3 (fig. 3) and case 8 (fig. 8). This phenomenon has occasionally been recognized in other records low in alpha wave content. Whether the effect is due to an increase or a decrease in the several gaseous elements supplied to the brain or is the result of release of "alpha wave inhibition" by release of the subject's concentration on himself or the test cannot be definitely stated.

During the sleep stage of the narcoleptic seizure it has commonly been observed that the control electroencephalogram gives way to a pattern of low amplitude, high frequency waves, which is subsequently superseded by predominantly low frequency, high voltage volleys. These discharges are entirely similar to the wave sequences observed during physiologic sleep. The congruity of these observations makes it apparent that the sleep component of the narcoleptic seizure is fundamentally a manifestation of physiologic sleep, albeit inappropriate.

Moreover, the unanimity in the observation of "sleep waves" almost mandates the acceptance of the term hypnolepsy, at least to designate the sleep component of the narcoleptic syndrome. However, since the sleep component is so overwhelmingly the primary presenting complaint of

5. Davis, H., and Wallace, W. M.: Factors Affecting Changes Produced in the Electroencephalogram by Standardized Hyperventilation, Arch. Neurol. & Psychiat. **47**:606-625 (April) 1942.

the patient, it seems entirely appropriate, as Foote [6] suggested in 1886, to designate the entire syndrome as hypnolepsy.

CONCLUSIONS

In a majority, 8 out of 10, of this series of cases of narcolepsy wave forms similar to those most commonly observed with the epilepsies were present.

Because of the unanimous objective electroencephalographic evidence that the primary component of the narcoleptic syndrome is a sleep phenomenon, it appears, despite the antiquity of the term narcolepsy, that the syndrome should be designated by the name of hypnolepsy (Foote [6]).

Since the electroencephalographic abnormalities observed during the interseizure phase of the hypnoleptic (narcoleptic) syndrome appear qualitatively similar to those associated with the epilepsies, it appears that Wilson's concept that the narcoleptic (hypnoleptic) syndrome is a member of the family of epilepsies is confirmed. A more precise statement of this relationship, based on electroencephalographic evidence, is that the clinical manifestations both in the epilepsies and in hypnolepsy are often associated with objective evidence of disturbances in the physiology of the brain.

6. Foote, A. W.: Narcolepsy, abstracted, Lancet **1**:25, 1887.

ACETYLCHOLINE TREATMENT OF SCHIZOPHRENIA

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The chief purpose of this paper is to report on the striking amelioration of a patient's schizophrenic illness following the administration of acetylcholine. The circumstances of the remission, if only in 1 case, seem to deserve report since their drastic and near catastrophic nature may throw some light on the mechanism of remission, not only with acetylcholine but possibly with other forms of shock therapy. The paper is also concerned with the effects of treatment with acetylcholine on 10 other patients with schizophrenia.

NEUROPHYSIOLOGIC EFFECTS OF ACETYLCHOLINE

Acetylcholine has been shown to have a stimulating effect at the myoneural junction, the parasympathetic endings, the sympathetic and parasympathetic ganglia and the cerebral cortex.[1] Intravenous injection of the drug in human beings is followed by convulsions associated with temporary cardiac arrest. In 8 epileptic patients Henderson and Wilson [2] observed various individual responses, namely, nausea, vomiting, intestinal peristalsis, sweating, changes in heart rate and fall in rectal temperature, immediately after cerebral intraventricular injection; other changes, which were not prominent, were flushing, sleep, variations in blood pressure, respiratory and pupillary changes, salivation and lacrimation. No motor phenomena were reported to have been produced in any patient.

The effect of acetylcholine on the blood vessels is of particular clinical interest because of the importance of vascular changes in production of neurophysiologic alterations. Wolff [3] observed that acetylcholine dilates the cerebral blood vessels; his studies have furnished the basis for the use of this drug in the treatment of epilepsy, though without success (Lloyd [4] and McLaughlin [5]). Electrocardiographic studies by Harris and Pacella [6] on psychotic patients clearly demonstrated bradycardia and cardiac arrest. Cardiac and respiratory irregularities and changes in blood pressure were reported (Bernheim and Bernheim [7]); it has been said that the respiratory changes are due to stimulation of chemoreceptor zones in the carotid sinus and the aortic arch and the inhibition of breathing partially to the effect of the drug on the respiratory center and the spinal cord (Schweitzer and Wright [8]). Gesell and Hansen [9] showed that slow intravenous injection of acetylcholine produced strengthening followed by weakening of respiration; abdominal, costal and accessory respiratory activities were affected independently.

The electroencephalographic observations include the demonstration of increased electrical activity of the cortex in the cat (Brenner and Merritt [10]) and in the rabbit (Miller, Stavraky and Woonton [11]). On the other hand, no electroencephalographic changes in the cat were observed by Chatfield and Dempsey [12] with acetylcholine alone, although specific changes were

From the Norwich State Hospital.

Presented at the Round Table on Shock Therapy at the meeting of the Connecticut Society of Psychiatry and Neurology, New Haven, Conn., Sept. 29, 1943.

1. Sollmann, T.: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1936, pp. 338-340.

2. Henderson, W. R., and Wilson, W. C.: Intraventricular Injection of Acetylcholine and Eserine in Man, Quart. J. Exper. Physiol. **26**:83, 1936.

3. Wolff, H. G.: The Cerebral Circulation: XI. The Action of Acetylcholine, Arch. Neurol. & Psychiat. **22**:686 (Oct.) 1929.

4. Lloyd, J. E. S.: Acetylcholine Therapy in Epilepsy, Brit. M. J. **1**:999, 1933.

5. McLaughlin, F. L.: Acetylcholine in Treatment of Epilepsy, Brit. M. J. **1**:997, 1933.

6. Harris, M. M., and Pacella, B. L.: Convulsant Shock Treatment of Patients with Mental Disease by Intravenous Injection of Acetylcholine, Arch. Neurol. & Psychiat. **50**:304 (Sept.) 1943.

7. Bernheim, F., and Bernheim, M. I. C.: Action of Drugs on the Choline Esterase of the Brain, J. Pharmacol. & Exper. Therap. **57**:427, 1936.

8. Schweitzer, A., and Wright, S.: Action of Prostigmine and Acetylcholine on Respiration, Quart. J. Physiol. **28**:33, 1938.

9. Gesell, R., and Hansen, E. T.: Eserine, Atropine and Nervous Integration, Am. J. Physiol. **139**:371, 1943.

10. Brenner, C., and Merritt, H. H.: Effect of Certain Choline Derivatives on Electrical Activity of the Cortex, Arch. Neurol. & Psychiat. **48**:382 (Sept.) 1942.

11. Miller, F. R.; Stavraky, G. W., and Woonton, G. A.: Effects of Eserine, Acetylcholine and Atropine on the Electrocorticogram, J. Neurophysiol. **3**:131, 1940.

12. Chatfield, P. D., and Dempsey, E. W.: Effects of Physostigmine and Acetylcholine on Cortical Potentials, Am. J. Physiol. **135**:633, 1942.

produced when acetylcholine and prostigmine were applied together. In psychotic patients Harris and Pacella [6] demonstrated abnormal, slow and high potentials which they asserted were a result of the vascular changes induced by primary cardiac arrest. This conclusion opposed the contention of Brenner and Merritt,[10] who stated that acetylcholine produces characteristic cerebral electrical response "by direct action on the nerve cells, fibers or synapses of the cortex." So-called epileptic discharges were reported by Williams [13] in epileptic patients, but "no charges of an epileptic character" were observed in normal persons.

ACETYLCHOLINE IN TREATMENT OF MENTAL DISEASE

In a search for convulsant drugs the efficacy of which would not be mitigated by the complications attending other shock therapies, notably fractures, Fiamberti [14] described his observations on acetylcholine. A report by Borgarello [15] indicated the usefulness of acetylcholine in insulin treatment in the presence of diminishing insulin resistance in some patients. Sandri [16] observed that in patients treated with acetylcholine there is a tendency to an increased sodium and a decreased magnesium content of the blood. The recent paper by Harris and Pacella [6] reported the therapeutic effects of acetylcholine on 8 patients, 6 women and 2 men. They were given from 3 to 61 treatments, with convulsant doses ranging from 220 to 600 mg. The investigators found that there was no ameliorating effect on the mental condition and concluded that this form of therapy "does not appear to be a desirable procedure." One patient made a prompt recovery after a course of a few electric shock convulsions, which were administered after an unsuccessful course of 31 injections of acetylcholine. No ill effects were observed even with large doses.

Our studies were carried out on 11 patients—7 women and 4 men. The injections of acetylcholine [17] were given intravenously as rapidly as possible. The dose in the first injection was 100 mg., and the amounts of the subsequent injections were increased in units of 50 mg. until a convulsion was produced. There was no evidence of the development of tolerance to the drug; in fact, the dose was sometimes decreased during the course of treatment without impairment of the convulsant effect. Generally larger amounts were necessary to produce convulsions in men than in women, probably because of the difference in weight. It was not felt necessary or desirable to restrain the patient during the seizure because the convulsion seemed so much more mild than that induced by metrazol or the electric current.[18] All injections were given in the morning to fasting patients; flatulence was common after an injection; voiding occurred occasionally, but defecation never took place. Most of the patients were reluctant to be treated, and it may be of interest that the patients who were subsequently given electric shock treatment displayed greater cooperation during such therapy.

DESCRIPTION OF SEIZURE

The following description is based on 27 instances in which a dose of 400 mg. was given and the effects were noted at fifteen second intervals.

Seven to ten seconds after injection the patient assumed a sitting position, with the knees drawn up to the chest, the arms flexed and the head bent forward. There were repeated violent coughs, sometimes with flushing. Forced swallowing and loud peristaltic rumblings could be heard. Respiration at this time was labored and irregular. Because of the continuous cough, the respiratory rate could not be determined adequately.

The coughing abated as the patient sank back in the bed. Forty seconds after injection the radial and the apical pulse were zero and the patient became comatose. At this time the pupils were dilated and reacted poorly to light. The deep reflexes were hyperactive. On some occasions a Babinski sign could be obtained.

In forty-five seconds the picture had become one of opisthotonos, abduction of the thighs, plantar flexion of the feet and pronation of the forearms, with opposition of the thumb and partial flexion of the fingers. At this time there was a brief period of apnea in some cases. Lacrimation, profuse perspiration and borborygmi were prominent. While the hypertonic state was developing there were occasional random movements of the limbs, sometimes slow, sometimes choreiform. The position of the limbs could be changed with little difficulty, and the new positions were frequently maintained. The deep

13. Williams, D.: Effect of Cholin-Like Substances on Cerebral Electrical Discharges in Epilepsy, J. Neurol. & Psychiat. **4**:32, 1941.

14. Fiamberti, A. M.: Sul meccanismo d'azione terapeutica della "burrasca vascolare" provocata con derivati della colina, Gior. di psichiat. e di neuropat. **67**: 270, 1939; Accessi a carattere epilettico provocati con l'introduzione sottoccipitale di sostanze vasodilatrici, Riv. sper. di freniat. **61**:834, 1937.

15. Borgarello, G.: Acetilcolina e insulinoterapia, Schizofrenie (supp.) **7**:83, 1939.

16. Sandrí, P.: Le variazioni del sodio e del magnesio del sangue nel trattamento convulsivante con acetilcolina della schizofrenie, Cervello **19**:64, 1940.

17. Dr. R. J. Floody, of Hoffmann-LaRoche, Inc., furnished the acetylcholine used in this investigation.

18. Atropine was kept on hand, but it was never used. One patient was given atropine ten minutes before the administration of acetylcholine, but no particular effect was observed.

reflexes were diminished or absent, and conjugate deviation was commonly observed. The deviation might be in any direction. The tonus then decreased, and the patient lay quietly in bed—cold, moist and gray.

In about ninety seconds flushing of the face marked the return of the pulse. The respiratory rate rose to 24 to 43 a minute. Coughing and gulping again became evident. Readings of the blood pressure obtained in the next minute or two showed an average fall in both the systolic and the diastolic reading of about 30 mm. (In 1 patient an increase in pressure was observed.)

Consciousness, as indicated by response to questions or by purposive activity, returned in one hundred and twenty-five seconds.

The patients tended to lie quietly in bed after the treatment. Sometimes they dozed lightly, but there was no evidence of stupor or confusion. Usually they could recollect the first phase of the reaction, and they complained of the early sensations of choking or burning in the throat.

In men a dose of 400 mg. did not usually produce a seizure of the severity seen in women.

RESULTS

The accompanying table presents the principal data concerning the 11 patients treated. All the patients were schizophrenic.

Data on Eleven Schizophrenic Patients Treated with Acetylcholine

Name	Sex	Age, Yr.	Duration of Illness	No. of Treatments	Outcome
F. B.	F	30	4 yr.	5	No change
J. H.	F	47	22 yr.	10	No change
E. K.	F	18	2 yr.	24	No change
M. B.	F	31	1 mo.	10	Slight improvement
L. G.	F	29	1 mo.	11	No change
R. S.	F	38	1 yr.	11	No change
M. Z.	F	40	3 mo.	19	Moderate improvement
J. M.	M	22	4 mo.	4	No change
M. C.	M	28	7 mo.	3	No change
B. K.	M	25	2½ yr.	3	No change
A. F.	M	36	4 mo.	4	Remission

From these data it can be seen that there were slight improvement in 1 woman, moderate improvement in another and complete remission in 1 man. In 8 patients no clinical change was observed; in 4 of these patients, to whom electric shock treatment has since been given, sufficient improvement has occurred to warrant their release from the hospital.

In the single patient in whom a remission occurred with acetylcholine, the effects were so striking that a more extensive presentation seems justified.

A. F., an Italian man aged 36, a mechanic by trade, got along moderately well financially until the onset of his illness. He was described as "temperamental," seclusive and sensitive. His intelligence quotient was 89, indicating dull normal intelligence. In January 1943 he began to complain that people were against him and that he was to be punished for something he had done. He became unusually quiet and seemed depressed; he could not sleep or eat and manifested marked indecisiveness. Hospitalization began in February 1943, with a clinical picture of persistent ideas of reference, delusions of persecution and auditory hallucinations. He made three suicidal attempts. In April 1943 he was transferred to the Norwich State Hospital. He manifested auditory hallucinations, insisting that he could hear the voice of Christ continuously telling him where he had been wrong in the past. He said that people knew all about him, especially about his previous perverse sexual acts, and expressed many ideas of guilt and sin. He was suicidal and made several impulsive attempts to kill or injure himself, such as butting his head against the wall or through a window.

Electric shock therapy was begun on April 19. A total of 24 treatments was given, the course being completed on June 11. At the end of the course of treatments no improvement was evident, although he seemed quieter and more cooperative. The same delusions and hallucinations were present. On June 22, eleven days after the completion of the electric shock course, he impulsively pushed his head through a window pane, sustaining a deep laceration of the chin. He explained that a voice had told him to do this. Treatment with acetylcholine hydrochloride was begun on July 17.

Acetylcholine Therapy.—The patient had four treatments, with increasing doses, as follows:

Date	Dose, Mg.
7/17	150
7/21	300
7/23	450
7/27	600

The usual minor responses were noted during the first two treatments. He was pulseless for twenty seconds during the third treatment, with some twitching. The fourth treatment is summarized as follows:

Fourth Treatment (7/27/43): The patient was apprehensive before the injection of 600 mg. of the drug at 9 a. m. A few seconds (two or three) after injection coughing, gasping (air hunger [?]), restless activity and twitching occurred. He became comatose, and the pulse was not obtainable for fifty seconds during this period. The blood pressure was 134 systolic and 88 diastolic. The pulse returned, and the pupils were noted to be contracted. He was heard to mumble some religious phrases. After twenty seconds he again became pulseless, this time for two minutes and twenty seconds. During this period the patient became very pale (grayish) and rigid for about half a minute; there then occurred a brief period of relaxation, followed suddenly by convulsive movements with opisthotonos lasting about a minute, during which he was first flushed and then cyanotic. The pupils were dilated. Toward the end of this phase the patient again became limp and pallid; the pulse then returned for five seconds, after which he was again pulseless for fifty seconds. During the next three minutes the pulse rate was as follows:

First minute	42
Second minute	52
Third minute	80

At this time there occurred much salivation and sweating, and breathing was so difficult that use of the accessory respiratory muscles was obvious. The blood pressure was 182 systolic and 110 diastolic. There was much gasping and moaning, but the comatose state persisted for approximately one hour. The pupils remained dilated for about forty minutes, with no reactivity to light. Toward the end of this phase the patient became extremely restless and made wild, incoordinated movements and many loud, unintelligible outcries, such as one often sees during hypoglycemic coma (insulin shock). There was no further salivation or sweating.

At 10:15 a. m., 50 cc. of 50 per cent dextrose was given intravenously, with no response. The patient remained unconscious. He began to regain consciousness at about 10:45 a. m. and seemed fully awake by noon. He said that he felt weak, but he was ambulatory by late afternoon. There was complete amnesia for the entire episode.

From the time of this treatment the patient persistently denied having any hallucinations or delusions. For a short time he continued to be somewhat preoccupied with matters pertaining to religion, as shown chiefly in his letters home. He became increasingly cheerful and optimistic about the future and spoke freely of having had "a lot of foolish ideas and imaginations." The complete amnesia for the last treatment continued, although he remembered well the apprehension and malaise associated with the previous treatments.

In late August he was allowed to go home for a week's visit. His family was much impressed by his condition and insisted that he had not been so well for over a year. They requested his release. By this time the patient's religious notions seemed to be no different from what one would expect of an average devout Catholic. When the patient was released, on September 15, he seemed entirely free from symptoms.

COMMENT

The value of a therapeutic agent depends on its efficacy and its safety as compared with other agents used for the same purpose. Considerable data are now available in the literature on the efficacy and safety of the insulin, metrazol and electric shock procedures; fewer data are available on picrotoxin, nikethamide and camphor. Gellhorn [19] suggested that the autonomic nervous system is chiefly concerned in the various forms of shock therapy. Our data, pertaining to the effect of acetylcholine on 11 patients, can be added to those gathered by Fiamberti [14] and by Harris and Pacella.[6] It is probably statistically unjustified to come to definite conclusions on the basis of so few cases, but it appears from the combined data that the relative therapeutic efficacy of acetylcholine therapy is slight and that its margin of safety may be relatively small. On the basis of our observations in 1 case the margin of safety between the convulsant and the lethal dose appears rather narrow. Nevertheless, we would point out that in some of our patients a 600 mg. dose produced no alarming changes and that Harris and Pacella reported no ill effects.

The question of the underlying mechanism in production of clinical remissions arises again in connection with our observations. Granted that our data are concerned with only 1 remission, we cannot dismiss it as an "accident." Why is one form of treatment effective in a given patient when another is not? Harris and Pacella reported on a patient who had a remission with electric shock treatment after failure with acetylcholine, whereas 1 of our patients had a startling remission with acetylcholine after failure with electric shock. Furthermore, 4 of our patients underwent remission or improvement with electric shock after failure with acetylcholine therapy. One might say that we did not always give a sufficiently extensive course of acetylcholine treatments, but this criticism could not be made of the courses given by Harris and Pacella, with negative results.

We do not presume to answer these questions except to indicate that our experience with all forms of shock treatment over the past seven years leads us to the opinion that damage to the brain (of a reversible or an irreversible sort) occurs. We would include our experience with frontal lobotomy. The diffuse hemorrhagic lesions observed in the brains of patients who have died after shock treatment of any sort indicate that in all patients there is probably induced, at least to some degree, the same pathologic process. Even in those instances in which the damage is reversible, a modified neurophysiologic status is established.

Under such changed conditions the "clinical picture" changes, at least in the sense that the productive symptoms often disappear, if only temporarily. We have never observed any definite alteration of affective flattening in schizophrenic patients by shock treatment. The poor prognosis, despite treatment, in cases of long-standing disease is generally accepted. It is common knowledge that as affective deterioration progresses the productive symptoms (hallucinations, delusions, excitement, stupor) disappear and that the typical deteriorated patient is essentially free of such symptoms. Here one is confronted with the paradox that the patient is better when he is worse. We apply the same paradox to the effects of shock treatment: The damage to the brain, through change in the neurophysiologic pattern of the patient's experiencing, makes the production of certain psychotic symptoms and signs less likely, perhaps in some patients impossible.

19. Gellhorn, E.: Autonomic Regulations: Their Significance for Physiology, Psychology, and Neuropsychiatry, New York, Interscience Publisher, Inc., 1943, p. 305.

We incline to the opinion that the consequence of such cerebral damage is the "artificial" production of affective flattening. The data [20] on the quieting effect of shock treatment on excited and overactive patients would bear this out. It is probable that prolonged hypoxia is basic to the damage to the brain.[21]

We conjecture that the changes in the brain induced by prolonged cardiac arrest with acetylcholine were at the basis of our patient's remission. The drug, apparently, has no other virtues —a small one, obviously, in the light of the near catastrophic consequences. Nevertheless, the fact remains that an almost immediate remission was produced, a clinical effect which was not obtained in any other patient. We consider that extensive damage to the brain was done in this patient and not in the others, despite comparable doses. Furthermore, we consider that this cerebral damage was of such a sort that obvious schizophrenic symptoms, at least for the time being, are impossible.

20. Cohen, L. H.: The Early Effects of Metrazol Therapy in Chronic Psychotic Overactivity, Am. J. Psychiat. **95**:328, 1938. Androp, S., and Green, E.: Résumé of Metrazol-Shock Therapy in Schizophrenia, Dis. Nerv. System **2**:222, 1941. Kubanek, J. L., and Ruskin, S. H.: Electrotherapy in Schizophrenia, J. Nerv. & Ment. Dis. **95**:698, 1942. Cohen, L. H., and others: Frontal Lobotomy in the Treatment of Chronic Psychotic Overactivity, Psychosom. Med. **4**:96, 1942. Reznikoff, L.: Comparison of Metrazol Convulsive Therapy with Electric Shock in Treatment of Schizophrenia, Arch. Neurol. & Psychiat. **49**:587 (April) 1943.

21. Himwich, H. E., and Fazekas, J. F.: Factor of Hypoxia in the Shock Therapies of Schizophrenia, Arch. Neurol. & Psychiat. **47**:800 (May) 1942.

SUMMARY

With 8 of 11 schizophrenic patients treated with convulsant doses of acetylcholine no general therapeutic benefit was obtained. In 1 patient there was slight, and in another moderate, improvement. One patient's condition underwent a dramatic remission after a therapeutic episode in which he was pulseless for such long periods that he was considered probably dead. On the basis of the available literature, it is considered that prolonged cardiorespiratory collapse occurred, as a consequence of which changes in the brain were produced.

The therapeutic results do not justify the continued use of acetylcholine in this manner, particularly since the margin of safety of the drug appears to be extremely slight.

Norwich State Hospital.

EFFECT OF SERUM ON SURVIVAL TIME OF BRAIN TISSUE AND REVIVAL OF CEREBRAL OXIDATION

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NEW YORK

Clinical experience with the use of blood transfusions [1] in the relief of irreversible insulin coma suggested the possibility that cerebral oxidation—the term is here used to denote oxygen uptake—may at times be depressed or suspended in vivo through the depletion or destruction of certain substances, other than oxygen or dextrose, contained in whole blood. The following in vitro studies were undertaken therefore to test the effect of certain constituents of the blood on the respiratory activity and survival time of brain tissue and the revival of cerebral oxidation after its spontaneous depression. I at first hoped to imitate the hypoglycemic effect by allowing the tissues to exhaust their own intracellular stores of carbohydrate and then attempting to revive the diminished oxidation at various intervals thereafter by the addition of dextrose, whole blood or serum. In preliminary trials the tissues showed a striking capacity to maintain their oxidation even in a dextrose-free medium for six or more hours before the oxidation fell off sharply. It was by no means certain, however, that the flattening of the oxidation curve which then occurred could be attributed to exhaustion of substrate, for in spite of a greatly accelerated rate of oxidation the presence of 200 mg. of dextrose per hundred cubic centimeters of immersion fluid made relatively little difference in the survival time of the tissue, and determinations of dextrose in the immersion fluid made after oxidation had practically ceased revealed a large excess of dextrose still available. Nor could the depression of oxidation be attributed to the development of a toxic inhibiting factor, since oxidation was not revived after the tissues had been washed in isotonic solution of three chlorides U. S. P. and placed in a fresh suspension medium. Inclusion of a small amount of fresh serum (0.25 cc. in 3 cc. of immersion fluid) effectively prevented any flattening of the oxidation curve within the limits of the duration of the experiment, i. e., twelve hours. The details of these experiments will now be described.

This study was aided by a grant from the Warner Institute for Therapeutic Research.

From the Psychiatric Division of Bellevue Hospital and the Department of Psychiatry of New York University College of Medicine.

1. Wortis, J., and Lambert, R. H.: Irreversible or Hyperglycemic Coma, Am. J. Psychiat. **96**:335, 1939.

METHOD

Minced whole brain tissue of adult white rats (over 5 months old and weighing over 200 Gm.) was used. In almost all the experiments less than half an hour elapsed between the decapitation of the rats and the beginning of the experiment. From 40 to 70 mg. of the minced wet tissue was weighed and immersed in 3 cc. of freshly prepared Krebs-Ringer phosphate solution [2] buffered at a p_H of 7.38 with various concentrations of dextrose, as indicated later. In the tipping

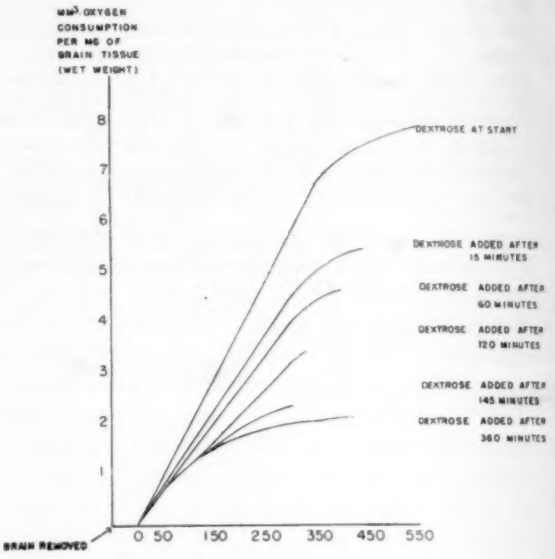

Fig. 1.—Effect of the addition of dextrose on the oxygen uptake of minced rat brain. Sufficient dextrose was added at each point to the dextrose-free suspension medium to bring the concentration of dextrose to 200 mg. per hundred cubic centimeters. There was no effective revival of oxidation after six hours.

experiments 2.5 cc. of immersion fluid was used in the main chamber with 0.5 cc. of additional solution in the side chamber containing enough dextrose to make a concentration of 200 mg. of dextrose per hundred cubic centimeters of immersion fluid after tipping. In the serum experiments 0.25 cc. of freshly prepared serum was added to 0.25 cc. of the Krebs-Ringer phosphate solution in the side chamber, or an equal amount was included in the central chamber at the start. Barcroft-Warburg manometers were used in a water bath at a temperature of 37 C. Strict cleanliness was observed, but a series of entirely aseptic experiments were included as controls, with the same results. Only occasional experiments in the twelve

2. The Krebs-Ringer phosphate solution has the following formula: sodium chloride, 90 Gm.; potassium chloride, 4.6 Gm.; calcium chloride, 3.6 Gm., and magnesium sulfate, 3.73 Gm., buffered with sodium phosphate and potassium acid phosphate.

hour runs were discarded because of contamination, signified by an extremely rapid oxygen uptake. The p_H was frequently checked, but no significant changes were observed. The data from each experiment involved readings from two to three manometers checked against at least two thermobarometers. All curves were based on averages from at least 10 such experiments.

RESULTS

The oxidation curve for minced brain in plain Krebs-Ringer phosphate solution flattened off in approximately six hours. The addition of dextrose to the suspension medium did not revive oxidation in the brain after this period. The addition of dextrose at various intermediate intervals resulted in an increased rate of oxygen uptake and longer survival of the tissue, in direct relation to the time that had elapsed before dextrose was added (fig. 1). If dextrose was present at the start, the rate of oxidation was almost doubled and the survival time prolonged several hours. Between the sixth and the ninth hour, however, an abrupt flattening of the oxidation curve took place, and the tissues died. This abrupt flattening did not occur (fig. 2) if a small amount of serum (0.25 cc.) was present in the suspension fluid, but oxidation continued at a

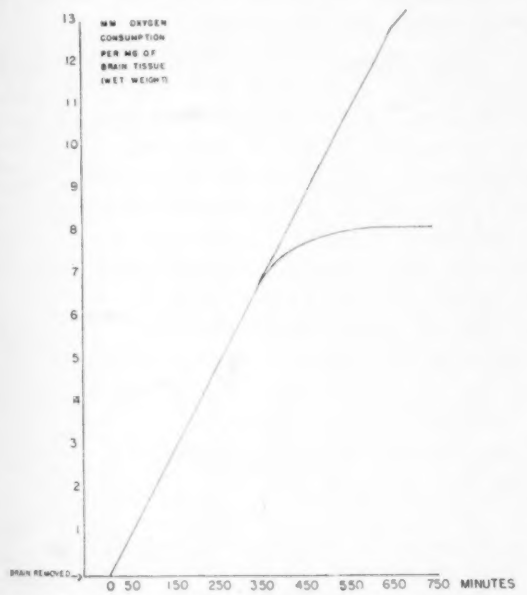

Fig. 2.—Two superimposed curves, showing the course of the oxygen uptake of minced rat brain with and without the presence of a small amount (0.25 cc.) of serum in 3 cc. of suspension medium containing 200 mg. of dextrose per hundred cubic centimeters. In the presence of serum, oxidation was maintained at a practically constant rate for the duration of the experiment (twelve hours).

practically constant rate for the duration of the experiment (twelve hours). In a dextrose-free medium the addition of a small amount of rat serum (0.25 cc.) at the end of six hours served to support the flagging oxidation and to promote the survival of the tissue (fig. 3). This effect was not enhanced by the addition of dextrose to the serum or by the use of whole blood.

COMMENT

The demonstration of the superior advantages of serum over Krebs-Ringer phosphate solution

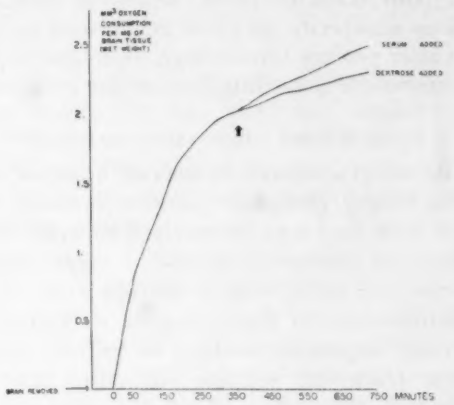

Fig. 3.—Effect of addition of a small amount (0.25 cc.) of serum to a dextrose-free suspension of minced adult rat brain. The addition of dextrose did not support the flagging oxidation. The addition of serum, of serum plus dextrose or of whole blood had the same effect in supporting the flagging oxidation.

as a medium for surviving tissues is not new and would make no claim to attention if the experiments did not serve to clarify some points in connection with the phenomenon. It is noteworthy that the presence of a small amount of serum in a dextrose medium did not accelerate the rate of oxidation, but greatly prolonged the maintenance of the metabolic activity of the tissue.

The apparent revival of flagging oxidation demonstrated in figure 3 is a similar phenomenon, for close analysis of the curves reveals that it is maintenance, rather than revival, of oxidative activity which is effected by the addition of serum. The possible explanations of the phenomenon are few: The amount of dextrose present in the serum cannot be considered a factor, and there is only the tenuous possibility that some other substrate is present in amounts sufficient to influence the metabolism of the tissues. A more likely possibility appears to be the presence in the serum of some essential element of the oxidative enzyme or catalyst system which is depleted or destroyed in the ordinary immersion fluid. Shaffer, Chang and Gerard [3]

3. Shaffer, M.; Chang, T. H., and Gerard, R. W.: The Influence of Blood Constituents on Oxygen Consumption in Nerve, Am. J. Physiol. **111**:697, 1935.

suggested some time ago that the large protein molecule of the serum served to maintain the normal permeability of the cell membrane.

The data of the experiments, together with clinical experience in the use of transfusions in cases of irreversible coma, may serve to throw light on the usefulness of serum in the revival of the flagging metabolism of the brain in some types of coma. It justifies further therapeutic trial with transfusions of serum or plasma in various nonspecific forms of coma, such as those seen after profuse hemorrhage, asphyxiation, carbon monoxide poisoning or vascular collapse.

SUMMARY AND CONCLUSION

The oxygen uptake of minced brain in plain Krebs-Ringer phosphate solution buffered at a p_H of 7.38 was approximately 0.85 cubic millimeters per milligram of tissue (wet weight) for the first hour, with a flattening off of the oxidation curve in approximately six hours. In a similar suspension medium of buffered Krebs-Ringer phosphate solution containing 200 mg. of dextrose per hundred cubic centimeters the oxygen uptake was 1.11 cubic millimeters per milligram of tissue for the first hour, with an abrupt flattening of the oxidation curve about eight hours afterward. This abrupt flattening did not occur if a small amount of serum was present in the immersion fluid, but oxidation continued at a practically constant rate for the duration of the experiment.

The cessation of oxidative activity of minced brain tissue was not due to lack of substrate, since determinations of the dextrose content of the immersion fluid revealed a substantial excess of dextrose still present after oxidations had practically ceased.

The addition of dextrose to a dextrose-free suspension medium did not revive oxidation in the brain after a period of six hours.

The cessation of oxidation in these experiments could not be attributed to the production of any inhibiting substance, since oxidation was not revived after the tissues had been washed in isotonic solution of three chlorides U. S. P. and placed in a fresh suspension medium.

There was a significant support of flagging oxidation on the addition of serum to a dextrose-free medium at the end of six hours. The effect was not enhanced by the combination with dextrose or by the use of whole blood.

The most likely explanation of the phenomenon appears to be the presence of some essential of the oxidative enzyme system in the serum or the restoration of normal osmotic relations by the large serum protein molecule.

50 Park Avenue.

INJURY TO THE PERONEAL NERVE DUE TO CROSSING THE LEGS

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NEW YORK

According to Spalteholz,[1] the common peroneal nerve usually branches from the sciatic nerve at the apex of the popliteal space. It runs along the medial margin of the biceps femoris muscle on the dorsal surface of the lateral head of the gastrocnemius muscle distad and laterad, and then behind the head of the fibula to the lateral margin of the shaft of the fibula, where it divides into its two terminal branches, the deep and the superficial peroneal nerve, both of which pass through the canal located in the origin of the peroneus longus muscle. The deep peroneal nerve innervates the tibialis anterior muscle and the extensor muscles of all the toes and supplies sensory fibers to the skin of the dorsal surfaces of the adjacent halves of the first and second toes. The superficial peroneal nerve innervates the peroneal muscles and supplies sensory fibers to the skin of the dorsal surface of the medial half of the big toe, of the dorsal surfaces of the adjacent halves of all the other toes, of the top of the foot and of the lower portion of the anterior surface of the leg. Dorsal flexion and eversion at the ankle and extension of all the toes are entirely dependent on these nerves.

Since the proximal portions of the deep and superficial peroneal nerves lie on the lateral margin of the shaft of the fibula and are covered only by a thin layer of soft tissue, they are vulnerable to injury by pressure. Persons who sit with their legs crossed in such a manner as to allow the upper third of the shaft of the fibula of the uppermost leg to ride against the head of the fibula of the lowermost leg commonly experience numbness and tingling on the top of the foot of the uppermost leg, due to compression of the superficial peroneal nerve between the two bones. Wilson [2] stated that, in spite of the frequency with which such sensations are produced in the leg or foot by sitting in a cramped way or with the legs crossed, reports of sleep palsies of the leg muscles due to nerve compression are rare as compared with similar injury to the radial or the ulnar nerve. The following case is an instance of bilateral injury to the peroneal nerve by habitual crossing of the legs.

REPORT OF A CASE

A physician aged 65 consulted me on June 29, 1942, complaining of foot drop on the left. He stated that five weeks previously, on his rising to his feet after reading in the sitting posture with his legs crossed, he had noted a sensation of numbness of the top of the foot and of the lower portion of the anterior surface of the leg on the left. Later that day the left foot began to slap the floor when he walked. Weakness at the left ankle increased, and several days later he almost fell down stairs when he turned his left ankle. Weakness and the sensation of numbness persisted, and a few days prior to the consultation he found an area of numbness on the top of the right foot when he was drying it with a towel but noted no weakness at the right ankle.

From the New York Hospital and the Department of Medicine (Neurology), Cornell University Medical College.

1. Spalteholz, W.: Hand-Atlas of Human Anatomy, translated by L. F. Barker, ed. 5, Philadelphia, J. B. Lippincott Company, 1900-1903, vol. 3, p. 782.

2. Wilson, S. A. K.: Neurology, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940, vol. 1, p. 345.

Fig. 1.—Photograph of the patient in his usual sitting posture, with the upper third of the shaft of the left fibula riding against the head of the right fibula. The areas of impaired sensation are outlined.

Fig. 2.—Photograph of the patient's legs, showing a dark area of skin over the upper third of the shaft of each fibula caused by the long-standing pressure.

Neurologic examination revealed abnormal signs only in the legs. The left foot slapped the floor when the patient walked. There was considerable weakness in dorsal flexion and in eversion at the ankle and in extension of all of the toes on the left. Fascicular twitchings were seen in the anterior muscles of the lower portion of the left leg. No weakness of the right leg could be found. There was no muscular wasting, and the knee, ankle and plantar reflexes were normal. Sensation to light touch and pinprick was decreased in the areas outlined in figure 1. Vibratory sense was also diminished over the left external malleolus.

The signs were clearly those of bilateral dysfunction of the peroneal nerve. On the left the deep and superficial branches of the common peroneal nerve were involved; on the right only the superficial branch was affected. Examination of the skin revealed an area of brownish induration, in which the hairs had been broken off short, over the upper third of the shaft of each fibula, indicating long-standing pressure directly over the proximal portions of the terminal branches of the common peroneal nerves. These cutaneous lesions are illustrated in figure 2. The patient stated that he had always sat with his legs crossed, more often with the left leg over the right than vice versa. At times he had noted that a foot had "gone to sleep." Figure 1 demonstrates his usual sitting posture, with the upper third of the shaft of the left fibula riding against the head of the right fibula. He explained that early in June 1942 he had taken some examinations, for which he had prepared continuously for six months. During this period he had spent three to four hours daily reading in the sitting posture with his legs crossed. Garters had not been worn during the last two months.

The patient was advised to stop crossing his legs and did so. Improvement was continuous. Six weeks later his gait was entirely normal. When he was last seen, about three months after the first examination, there was barely perceptible weakness in dorsal flexion and in eversion at the ankle and in extension of the big toe on the left, and the areas of impaired sensation had receded about four fifths of their original size. The marks of pressure on the legs had almost disappeared.

CONCLUSION

The almost universal habit of sitting with the legs crossed may cause injury to the peroneal nerve.

525 East Sixty-Eight Street.

PROGRESSIVE MULTIFORM ANGIOSIS

ASSOCIATION OF A CEREBRAL ANGIOMA, ANEURYSMS AND OTHER VASCULAR CHANGES IN THE BRAIN

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BRENTWOOD, N. Y.

Knowledge of the growths originating from the blood vessels of the brain is still limited and confused. No doubt the monograph of Cushing and Bailey [1] and other recent works (Bergstrand,[2] Northfield [3]) have helped greatly to clarify this interesting chapter of neuropathology. However, the relative rarity of these conditions also limits their study, so that further contributions have to be anticipated. This consideration justified in our opinion the report of a case presenting a cerebral angioma, a huge aneurysm of the circle of Willis, diffuse alterations of the subarachnoid vessels and an aneurysm of the abdominal aorta. It was felt that the study of this peculiar association could throw additional light on the subject.

REPORT OF A CASE

History.—The family history was without significance. The patient was born in 1884 in the United States, of Irish-American parentage. No disturbances of behavior or neurotic traits were present during childhood. At the age of 12 years he was struck on the head with the shaft of a wagon. No details are available concerning either the immediate result or the after-effect of the injury. At the age of 17 he began to have convulsions, on the average of two or three a year. At the age of 28 he started to drink and since then had had several attacks of dipsomania. In July 1936 he began to drink even more excessively. He had occasional visual hallucinations and borrowed money from his friends and neighbors, spending all he could get his hands on for alcohol.

Examination on Admission.—The patient was admitted to Pilgrim State Hospital on Sept. 28, 1936 on account of addiction to alcohol and disorderly behavior. Physical examination on admission revealed slight enlargement of the heart and chronic bronchitis. The pupils reacted sluggishly to light. The knee jerk was diminished and the ankle jerk absent on both sides. Routine laboratory tests gave normal results. The Wassermann reaction of the blood was negative. Nothing outstanding was noted in examination of the mental status. Behavior and mood were not disturbed. No delusional or hallucinatory material could be elicited. The patient was well oriented as to time, place and person; memory was excellent, and retention and immediate recall were good when he made a real effort. His intelligence was average. The diagnosis was "psychosis due to alcohol, confusional syndrome." About a month later he was paroled. No epileptic seizures occurred in this period.

Subsequent Course.—The patient was returned to Pilgrim State Hospital in January 1937 with a history of having started to drink heavily after New Year's. He again made a satisfactory adjustment in the hospital and was paroled in July 1937. After this, for about three years, he was in and out of the hospital several times. In April 1938 paralysis of the left superior rectus and left inferior oblique muscles was observed.

The patient's last admission was in April 1940. At that time examination of the eyegrounds revealed bilateral optic nerve atrophy, and the visual fields showed bilateral nasal hemianopsia. Since then the patient had had seizures at irregular intervals, and his mental status had deteriorated steadily. On account of increasing weakness, he was put to bed on Feb. 10, 1943. On the evening of March 10 he had three grand mal attacks. He remained in an unconscious state the following day, then rallied to a point where he was able to take some fluid and to speak to relatives who came to see him. The temperature ranged from 101 to 104 F. The pulse rate varied from 90 to 120 and the respiratory rate from 24 to 32 per minute. The signs in the chest were consistent with a diagnosis of bronchopneumonia.

On March 15 he lapsed again into coma and died at 5:40 a. m.

Necropsy.—Brain: The brain weighed 1,630 Gm. Nothing unusual was noticeable on the external surface of the dura. On removal of the dura no clouding of the leptomeninges was apparent except for a local area, to be mentioned later. The convolutions showed no appreciable change. It was observed that the blood vessels over the surface of both hemispheres were enlarged, thickened and much more prominent than usual (fig. 1). In certain areas they appeared to be increased not only in volume but in number. It was often difficult to determine the nature of these vessels. In the frontal lobe, for instance, vessels which had the appearance of arteries opened instead into the superior longitudinal sinus. At the terminal part of the left lateral cerebral fissure one noted two large, thickened vessels, which were directed toward the superior

From the Department of Pathology of Pilgrim State Hospital.

1. Cushing, H., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C Thomas, Publisher, 1928.

2. Bergstrand, H.: On the Classification of the Haemangiomatous Tumours and Malformations of the Central Nervous System, Acta path. et microbiol. Scandinav., 1936, supp. 26, pp. 89-95.

3. Northfield, D. W. C.: Angiomatous Malformations of Brain, Guy's Hosp. Rep. **90**:149-170, 1940-1941.

parietal lobule (fig. 2). The most anterior of these two blood channels was located immediately caudal to the posterior central gyrus; the posterior vessel ran through the supramarginal gyrus and the angular gyrus and finally reached the superior parietal lobule, near the transverse occipital sulcus. In the superior parietal lobule these two vessels gave off minor branches in such numbers as to constitute a true angioma. The vessels of the angioma had a tortuous and interwoven course. This network covered the entire surface of the lobule and expanded medially into the precuneus. The arachnoid covering the angioma was thickened and clouded, so that the visibility of the individual vessels was limited (figs. 1 and 2).

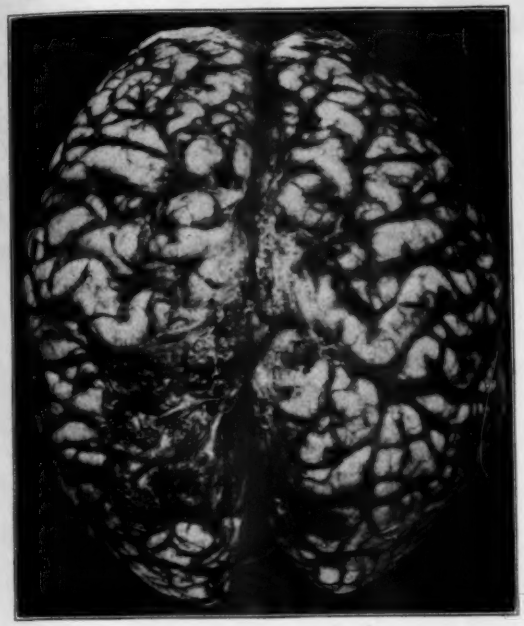

Fig. 1.—Dorsal view of the brain. All the vessels are enlarged and thickened. Note the angioma on the left parietal lobe. (A thickening of the arachnoid limits there the visibility of individual vessels.)

Fig. 2.—Left oblique view of the brain. Two large ascending vessels give rise to the angioma in the left parietal lobe (described in the text).

When the brain was cut in coronal sections, it was noted that the lesion projected deep into the parietal lobe (fig. 4*A*). It measured 5 by 3.5 by 3.8 cm. In the vicinity other, small clusters of enlarged vessels appeared in the subarachnoid space.

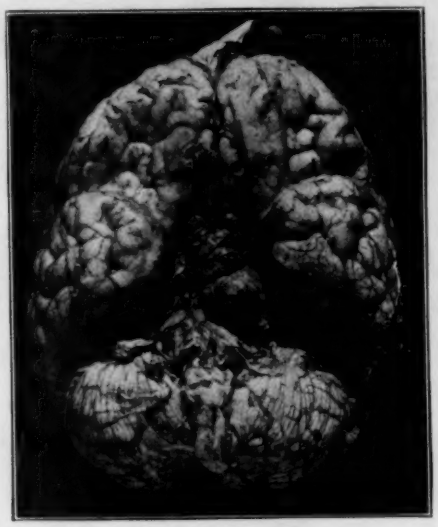

Fig. 3.—Ventral view of the brain, showing a large aneurysm. (The incisions in the aneurysm were made at necropsy.)

Fig. 4.—*A*, frontal section of the left parietal lobe passing through the center of the angioma. *B*, aneurysm after removal from the brain.

On the basal aspect of the brain an aneurysmal dilatation was noted on the left side of the circle of

Willis (fig. 3). This aneurysm was remarkably large and included the posterior communicating artery and short portions of the posterior cerebral and internal carotid arteries on the same side. Its anteroposterior diameter was about 5 cm. and its transverse diameter about 3.5 cm. It compressed the optic chiasm, the mamillary bodies, the cerebral peduncles, the posterior perforate substance and the left half of the pons. The basilar artery was not involved. When the aneurysm was isolated (fig. 4 *B*), its surface was seen to be divided in two masses by a sulcus, which probably corresponded to the junction of two vessels. The larger of these masses was the caudal and the smaller the frontal portion. Dorsal to the caudal mass was a

Fig. 5.—General view of the central part of the angioma. Hematoxylin and eosin; × 25.

Fig. 6.—*A* (× 55), gigantic vessel, showing splitting of the elastica. *B* (× 25), enormous vessel, showing varied appearance of the elastica, which at certain points maintains the normal escalloped aspect and at others shows a more or less rectilinear course of splitting. Weigert stain.

third, small, spherical mass. Section of the aneurysm revealed that it was completely occluded by a thrombus. The entire aneurysm had a capacity of 27.5 cc., as measured by the volume of replaced water.

Other Organs: Many areas of consolidation were noted in both lungs. There was an aneurysm, measuring 4 cm., in the abdominal aorta. An undescended testicle was observed in the abdomen.

Microscopic Examination.—Angioma: Hematoxylin and eosin preparations of sections from the lesion in the left parietal lobe disclosed that it consisted of blood vessels and little interstitial tissue. The vessels seemed to originate in the subarachnoid space, dipping into the fissures and sulci which separate the cerebral convolutions. Because of their number and size, they compressed the convolutions in such a way as to leave little nerve tissue between the vessels from two neighboring sulci. The vessels were of various sizes and presented numerous irregularities. Many of them were gigantic and conferred to the tissue a cavernous aspect (fig. 5). Medium-sized vessels were less numerous. Capillaries and precapillaries were seen only in a few zones, in particular where meningeal tissue was recognizable.

The large vessels presented the most irregular forms, with constrictions and dilatations. Projections of the wall into the center of the vessels were as frequent as outward projections. Aneurysmal outpocketings of the vessels were also frequently observed. The irregularities in the circumference of the blood channels were due either to the tortuous turning of the vessel or to the difference in thickness in various parts of the wall.

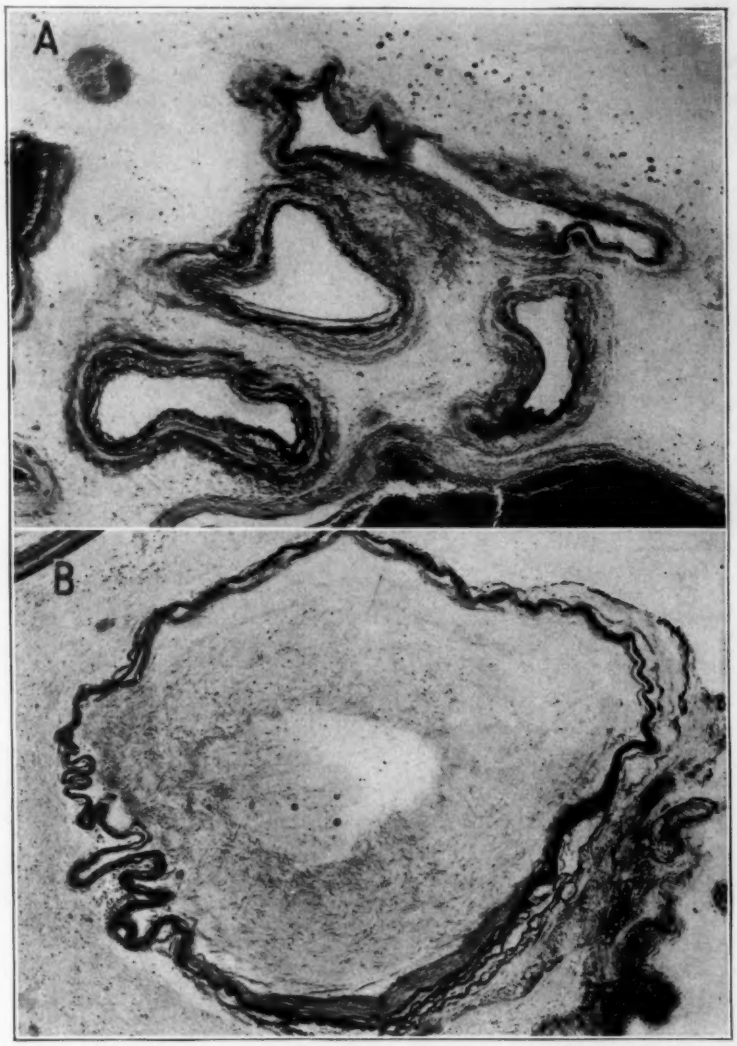

Fig. 7.—*A*, group of vessels, showing various stages of the process of arteriolization. *B*, course of the elastica, following the irregularities of the vascular wall. Weigert stain; × 55.

Vessels of medium size presented the same irregularity of form, but less frequently and in a less pronounced manner.

The nature of the vessels was not always easy to determine in hematoxylin and eosin sections. In these preparations, however, the veins seemed to outnumber the arteries.

The intima presented various characteristics. At times it consisted of a single row of flattened cells, but as a rule it was conspicuously thickened. At times this intimal proliferation was equally pronounced throughout the circumference of the vessel, but oftener it was

particularly prominent in certain spots, forming the aforementioned nodules projecting into the lumen (fig. 8*B*). Proliferation of the intima to such an extent as entirely to occlude the vessel was only exceptionally observed. The presence of swollen endothelial cells lining the lumen was noted frequently, and almost exclusively in veins (fig. 8*A*). These swollen endothelial cells contained droplets of fat. In Van Gieson sections the thickened intima appeared to contain numerous collagen fibers. Weigert sections revealed the presence of an elastic interna in many vessels and (fig. 7*B*). Thickening of the elastica was frequently encountered, but far more frequent was the splitting of this membrane in several layers (fig. 6*A* and *B*). Many vessels did not have a definite elastic membrane but showed numerous elastic fibers running concentrically in the intima. These fibers were often gathered together in certain points of the circumference and gave the impression of forming there a real elastic membrane (fig. 7*A*). This phenomenon, referred to by many authors as a process of arteriolization, was frequently observed in this case. Not seldom, however, the elastic fibers were seen leaving the intima and invading the other coats. At times they were of such quantity that in Weigert sections the entire width of the three coats appeared as a network of elastic fibers. The media also appeared thickened. Often this tunica also participated conspicuously in the formation of the inward projections already described. Van Gieson and Mallory stains for connective tissue revealed the presence of smooth muscle cells in the media, but these muscular elements were by no means numerous.

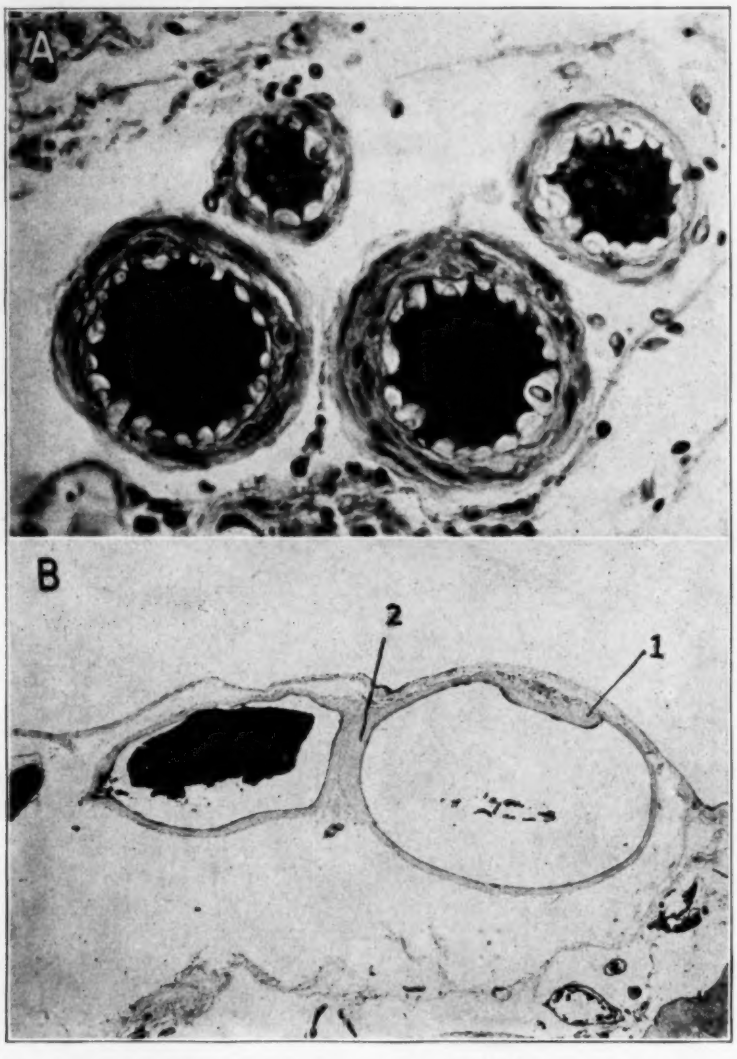

Fig. 8.—*A* (× 325), group of vessels, showing swelling of the intimal endothelial cells and projection into the lumen. *B* (× 5), enlarged subarachnoid veins of the right frontal lobe. Note two intimal thickenings of one vessel. At *1* the nodular thickening projects into the lumen; at *2* the thickening extends centrifugally. Hematoxylin and eosin stain.

established in this way the arterial nature of many blood channels which in hematoxylin and eosin preparations had the appearance of veins. In many vessels, especially those of medium size, the elastic membrane had the normal tortuous, escalloped appearance. In other vessels, especially those of gigantic size, the elastica had at times a relatively rectilinear course, probably due to lack of efficient contraction of the tunica media; at other times it was tortuous, following all the irregularities of the vascular circumference

Connective tissue, collagen and elastic fibers were the chief constituents of this tunica.

The adventitia appeared generally enlarged, but not so much so as the intima and the media.

Retrogressive and degenerative characteristics were not important features in the vascular elements of this lesion. Hyaline degeneration of the vascular walls was not seen. Calcification of the walls was observed in a few sections.

The interstitial tissue surrounding the vessels offered also several points for consideration. In the most superficial part of the lesion this tissue was seen as a continuation of the leptomeninges lining the cerebral cortex. As a matter of fact, a few typical psammoma bodies were observed in it. The connective tissue nature of this interstitial tissue was easily recognized in sections stained by Van Gieson's method and with Mallory's aniline blue. It consisted chiefly of fibroblasts and collagen fibers. However, in the deepest salients of the lesion it was possible to distinguish two sharply differing components of the interstitial tissue —connective and glial tissue. The glial elements could be easily distinguished from the connective tissue in sections stained with Mallory's aniline blue. As already mentioned, normal parenchyma of the brain was seen between groups of vessels in the deepest part of the lesion. In this parenchyma calcification of capillaries was often observed (fig. 9 *A*). At times the calcification was advanced and involved the entire wall of the capillaries; often it was still incomplete, the capillaries appearing to be covered by numerous black dots.

Meningeal Vessels: Examination of the vessels lying in the subarachnoid spaces over all the lobes of the brain led to the conclusion that few vessels could be considered in normal condition. On the other hand, the vascular alterations were seldom as pronounced as those described in the angioma. The vessels appeared almost always enlarged. The thickening of the walls was less conspicuous and more uniform than that in the vessels of the angioma. However, nodules of the media and intima, identical with those already described, were encountered, even in vessels located at a great distance from the angioma, such as those in the right frontal lobe (fig. 8 *B*). Another interesting characteristic was the larger proportion of veins to arteries than was observed in the angioma. As a matter of fact, Weigert sections did not reveal any elastic interna or traces of elastic tissue in a great number of these vessels.

Swelling of endothelial cells lining the lumen was observed in several vessels, especially the veins. A few vessels were occluded by thrombi which were undergoing organization. In rare cases recanalization was observed.

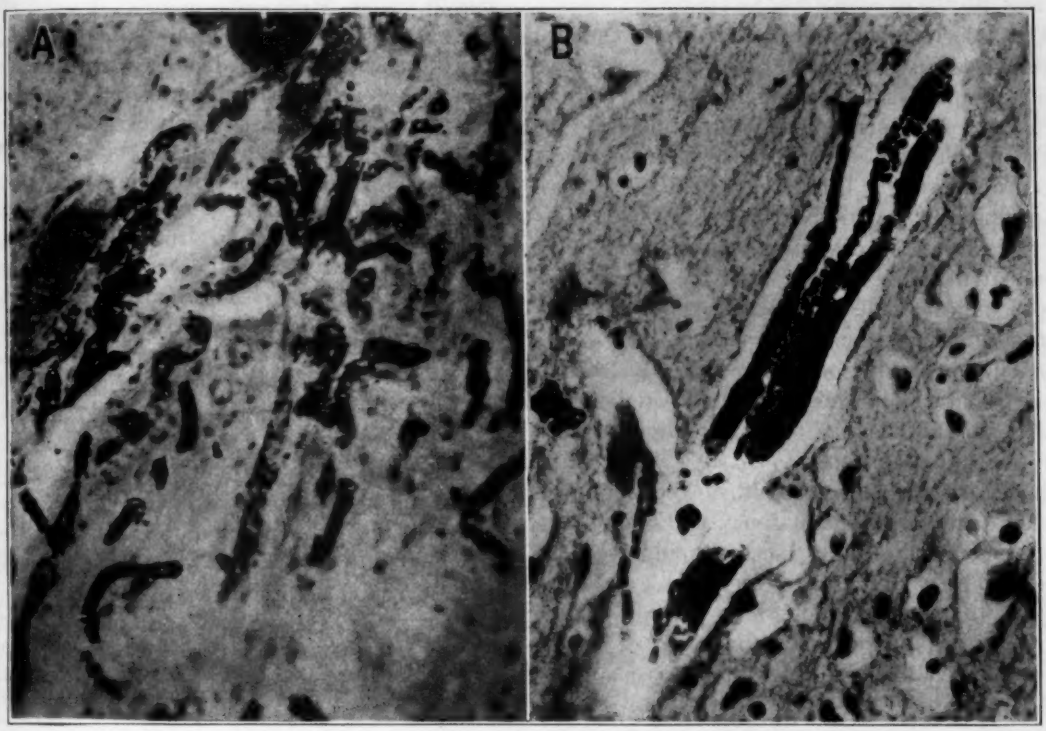

Fig. 9.—*A* (× 50), calcified cerebral capillaries; *B* (× 300), brushlike proliferation of cerebral capillaries. Hematoxylin and eosin stain.

Cerebral Vessels: In most of the regions of the brain there were no appreciable vascular changes. On the other hand, in several areas an increased number of capillaries in the cortex and in the white matter was noted in hematoxylin and eosin sections. However, such an increase may have been more apparent than real and may have been due to the fact that the capillaries were engorged with blood and therefore much more apparent.

The Eros stain for vascular pattern[4] did not reveal any change in the network of capillaries in these areas, except for the occasional presence of brushlike formations of capillaries detached from a common trunk at an acute angle and running parallel with one another.

4. Eros, G.: Method for Fuchsin Staining of the Network of Cerebral Blood Vessels, Arch. Path. **31**: 205-219 (March) 1941.

These brushlike formations, considered by Cerletti [5] as evidence of "absolute aggregate vascular proliferation" and interpreted in the same way by Eros and Priestman,[6] were at times so evident that even in hematoxylin and eosin sections they could be clearly seen (fig. 9*B*). In a few areas, located in the vicinity of the angioma, groups of capillaries appeared calcified, as previously described.

Aneurysm: The walls showed great irregularity in thickness. It was not possible to recognize the three vascular coats. The walls consisted of connective tissue, and in some points of a homogeneous, hyaline-like structure. Calcareous deposits were frequently encountered. No remnants of elastic tissue were noted at any point in sections stained by the Weigert or other methods. No inflammatory changes were noted. The aneurysm contained an organizing thrombus.

COMMENT

The association in the same case of a cerebral angioma, diffuse vascular abnormalities in the brain, an aneurysm of the circle of Willis and an aneurysm of the abdominal aorta stimulates certain considerations. Such an association seems to substantiate the belief that the lesions were congenital and suggests the term malformations for the alterations described. However, careful examination and comparison of the intracranial lesions indicate that they were capable of modification and had acquired some neoplastic qualities. There is no doubt that the diffuse anomalies of the subarachnoid vessels and the angioma of the left parietal lobe had the same origin. However, the latter appeared to be at a much more advanced stage. The vessels of the angioma, although presenting qualitatively the same characteristics as the other subarachnoid vessels, were more enlarged and irregular, and the process of arteriolization had already taken place, or was taking place, in many of them. These observations indicate that the subarachnoid vessels, or group of vessels, probably would have formed other angiomas if the patient could have lived long enough. In addition, it seems that these lesions are not genuine static malformations but are capable of further development, differentiation and autonomous growth. We are therefore inclined to agree with Bergstrand,[2] who stated that the attempts to classify the vascular growths of the nervous system "as either tumours in the narrow sense or as malformations are bound to be misleading because the two conceptions do not exclude each other."

Although we agree with the statement of Turner and Kernohan [7] that the mode of progression of the angiomas is through enlargement of the individual vessels, we cannot agree with them in their assertion that this enlargement is due to static changes or to changes in the dynamics of the blood circulating through the vessels. The process of progressive arteriolization discloses that these vessels not only enlarge but differentiate. They seem, therefore, to have an inherent potentiality for development and growth.

The presence in this case of two aneurysms is of great interest and must be considered in relation to the pathogenesis of the condition. Tuthill [8] and McDonald and Korb [9] observed that such lesions are generally due to an arteriosclerotic process, and Maass [10] reaffirmed that their origin is to be attributed to a syphilitic infection. Eppinger,[11] as far back as 1887, noted that congenital structural defects are antecedent to formation of aneurysms. Forbus [12] attributed the formation of aneurysms to "weak spots," similar to those observed in the muscular coat of blood vessels in the brains of children. Globus and Schwab [13] expressed the opinion that inherent defects and superimposed acquired pathologic processes are complementary factors in the production of aneurysm. One of us (Arieti [14]) described a case of multiple meningioma associated with an intracranial aneurysm. We have recently observed a case in which an acoustic neurinoma and a popliteal aneurysm were presented. The last-mentioned observations [15] seem to support the view that often an ontogenetic defect is a fundamental factor in the formation of

5. Cerletti, U.: Die Gefassvermehrung in Zentralnervensystem, in Nissl, F., and Alzheimer, A.: Histologie und Histopathologie, Jena, Gustav Fischer, 1910, vol. 4, p. 77.

6. Eros, G., and Priestman, G.: Cerebral Changes in Carbon Monoxide Poisoning, J. Neuropath. & Exper. Neurol. **1**:158-172 (April) 1942.

7. Turner, O. A., and Kernohan, J. W.: Vascular Malformations and Vascular Tumors Involving the Spinal Cord: A Pathologic Study of Forty-Six Cases, Arch. Neurol. & Psychiat. **46**:444-463 (Sept.) 1941.

8. Tuthill, C. R.: Cerebral Aneurysms, Arch. Path. **16**:630 (April) 1933.

9. McDonald, C. A., and Korb, M.: Intracranial Aneurysms, Arch. Neurol. & Psychiat. **42**:298-328 (Aug.) 1939.

10. Maass, U.: Die Syphilis als häufigste Ursache der Aneurysmen an der Gehirnbasis, Beitr. z. path. Anat. u. z. allg. Path. **98**:307-322, 1937.

11. Eppinger, H., cited by Globus and Schwab.[13]

12. Forbus, W. D.: On the Origin of Miliary Aneurysms of the Superficial Cerebral Arteries, Bull. Johns Hopkins Hosp. **47**:239-284 (Nov.) 1930.

13. Globus, J. H., and Schwab, J. M.: Intracranial Aneurysms: Their Origin and Clinical Behavior in a Series of Verified Cases, J. Mt. Sinai Hosp. **8**:547-578 (Jan.-Feb.) 1942.

14. Arieti, S.: Multiple Meningioma and Meningiomas Associated with Other Brain Tumors, J. Neuropath. & Exper. Neurol., to be published.

15. Eppinger.[11] Forbus.[12] Globus and Schwab.[13] Arieti.[14]

aneurysms. At times this defect may be considered responsible for associated lesions, such as tumors. This point of view is corroborated by the observations in this case. As a matter of fact, it is almost impossible to explain the association of two aneurysms with the other vascular lesions as purely coincidental. On the other hand, it seems logical to attribute all the lesions to one ontogenetic disorder, which in this case was limited strictly to the vascular system.

The lesions in this case having all been recognized as expressions of a pathologic entity, the problem is now to determine whether this picture can be included in the present classifications of the vascular disorders. As a matter of fact, the term angioma arteriovenosum would refer only to the lesion of the left parietal lobe. The term angiomatosis, used by Lévy,[16] Panara [17] and others, although including the angioma and the other alterations of the subarachnoid vessels, would not include the aneurysms. We cannot consider this case as representing a form, even abortive, of Sturge-Weber disease, if we accept the definition of this disease given by Bergstrand [2] and Northfield.[3] The condition can by no means be identified with Lindau's [18] disease or with the syndromes described by van Bogaert,[19] Zeldenrust,[20] Snapper and Formijne [21] and others. It must be included, however, in the group of mesodermal or ectomesodermal dysplasias to which Recklinghausen's neurofibromatosis, Lindau's disease, the Sturge-Weber syndrome and, as recently reemphasized,[22] tuberous sclerosis probably belong. For the syndrome presented by our case we propose the term "progressive multiform angiosis."

16. Lévy, G.: L'angiomatose du système nerveux central, Presse méd. **38**:37-40 (Jan. 8) 1930.

17. Panara, C.: Contributo alla conoscenza dell'angiomatosi cerebrale, Riv. di neurol. **7**:579-606 (Oct.) 1934.

18. Lindau, A.: Studien ueber Kleinhirncysten: Bau, Pathogenese und Beziehungen zur Angiomatosis retinae, Acta path. et microbiol. Scandinav., 1926, supp. 1, p. 128.

19. van Bogaert, L.: Angiome caverneux du strié et malformations viscérales multiples, Rev. neurol. **71**: 734-737 (June) 1939.

20. Zeldenrust, J.: Case of Angiomatoses cerebri, Am. J. Cancer **34**:234-239 (Oct.) 1938.

21. Snapper, I., and Formijne, P.: Anevrysmen baseos cerebri en cysternieren, Nederl. tijdschr. v. geneesk. **82**:5664-5669 (Nov. 26) 1938.

SUMMARY

In the case reported the clinical picture was one of epileptic seizures, periodic disorderly behavior, dipsomaniac attacks and progressive mental deterioration. Autopsy revealed an arteriovenous angioma of the left parietal lobe, diffuse alterations of the subarachnoid vessels, a huge aneurysm of the circle of Willis and an aneurysm of the abdominal aorta. The subarachnoid vessels and the blood vessels of the angioma presented various stages of the "process of arteriolization" and other alterations. Calcification and brushlike proliferation were noted in cerebral capillaries.

In view of the observations in this case, we conclude:

1. No sharp distinction is possible between vascular malformations and vascular tumors of the brain.

2. Congenital defects may be a fundamental factor in the formation of cerebral and other aneurysms.

3. All the vascular lesions present in this case probably belong to but one pathologic entity.

On account of the difficulties of including the syndrome presented in this case in the modern classifications of the vascular disorders, the term "progressive multiform angiosis" is proposed.

Mr. R. Schilling gave technical assistance.

Pilgrim State Hospital.

22. Ross, A. T., and Dickerson, W. W.: Tuberous Sclerosis, Arch. Neurol. & Psychiat. **50**:233-257 (Sept.) 1943.

Obituaries

ROY DENNIS HALLORAN, M.D.
1894-1943

The death of Roy Halloran interrupted the development of a fine personality in the midst of its most productive period. He had recently been called to the post of chief of neuropsychiatry for the Medical Department of the United States Army, stationed in the Surgeon General's Office. His became the task of organizing and implementing with qualified personnel a branch of the Medical Department of the Army which has assumed a peculiarly critical importance during this war. No one could have shown better adaptability to the exigencies of emergent situations or more administrative competence or ability as team worker and team builder than did Roy Halloran. These qualities made him eminently suited to the task which had to be performed as a part of the immense and, perforce, cumbersome administrative machinery of an army in the process of building during a total war.

Colonel Halloran was born in Cambridge, Mass., Aug. 4, 1894. He received his degree of Bachelor of Arts from Dartmouth College in 1917 and his degree of Doctor of Medicine from Columbia University College of Physicians and Surgeons in 1920. While still a medical student he became interested in clinical and administrative psychiatric work. After serving his internship at the Newark City Hospital, he was assistant physician at the New Hampshire State Hospital and, later, at the Boston State Hospital, where he became assistant superintendent in 1928. It was here that, under the guidance of Dr. James V. May, then superintendent of the hospital, he developed as a psychiatrist and administrator. It was here, also, that, under the influence of Dr. Abraham Myerson, he became interested in teaching and investigative work. He collaborated with Dr. Myerson in the studies of cerebral metabolism and made with him a notable contribution in the development of the method of jugular venepuncture. This work became widely known in this country and abroad. He also published several papers on the administrative and social aspects of psychiatry.

In 1929 he became assistant to the commissioner of the Department of Mental Diseases of Massachusetts and in 1933 became first superintendent of the Metropolitan State Hospital. During the nine years of his administration of this hospital, his abilities and personal qualities found their full expression. The conspicuous characteristic of his administrative methods was the courage with which he steered the development of the hospital along the line of research and teaching. He made it an educational community center for mental hygiene. He never hesitated to support and promote new ideas in the matter of utilization of hospital facilities for these purposes. He was always anxious to build and stimulate the spirit of professional dignity among members of the medical staff, and he made special efforts to induce them to have interests outside the narrow field of their routine daily activities. He detested gossip and mental stodginess, for the growth of which the closed institutions offer a propitious ground. He promoted investigative work at the hospital and prompted members of his medical staff to establish affiliations with other academic establishments and medical schools. He endeavored to offer the hospital facilities to these schools for lectures, clinical demonstrations and training of students and interns.

His inherent ability in building the spirit of teamwork about him was one of his great assets. To this, no doubt, he chiefly owed his accomplishments as administrator and organizer. This quality of his manifested itself in all phases of hospital activities. With Dr. Salomon Gagnon, then assistant superintendent, he was one of the first, if not the first, to establish a hospital library directed by a trained librarian, not merely as a diversional, but as a deliberately therapeutic, facility. The books were selected for the patients according to the therapeutic indications of their mental states. He promoted the department of occupational therapy, not merely as a routine to keep the patients out of mischief but as a means of providing an outlet for creative self expression. The exhibits of patients' paintings, sculptures, woodwork and carvings, held annually at the hospital, became in a sense a social event, with all the atmosphere of the *vernissage*. By these public exhibits, and by theatricals, shows and garden parties, he wished to bring the professional and the lay public to the hospital in order to break, as much as possible, the wall of

psychologic and social isolation of the patients in the hospital. This is generally done; yet his efforts in this direction were especially effective.

In 1936, under the impetus given by the establishment of the American Board of Neurology and Psychiatry, he founded postgraduate seminars in basic subjects pertaining to the specialty. Characteristically, he himself attended the lectures of the first seminar, with a small group of physicians who came from other psychiatric hospitals and from the community. Once he became convinced of the potential value of these seminars, he did not spare his efforts in promoting them and in providing all the necessary facilities for their development. Since the first one the seminars have been held annually, and nearly 400 graduate physicians from Massachusetts and neighboring states of New England have availed themselves of this educational facility. The Collected Lectures of the Seventh Seminar (1941-1942) on Military Neuropsychiatry, General Psychiatry and General Neurology, published under his direction by the Metropolitan State Hospital, found many appreciative readers among physicians, especially those in military service.

With such likable personal qualities and special abilities, it was not surprising when, in August 1942, he was called to Washington, D. C., to assume duties as chief of the neuropsychiatry branch of the Surgeon General's Office. He answered this call to a new and responsible position as a matter of duty to his country. To these duties he gave, as ever, all of himself. He died of coronary thrombosis on Nov. 10, 1943 and is buried at the Arlington National Cemetery.

PAUL I. YAKOVLEV, M.D.

Abstracts from Current Literature

Anatomy and Embryology

AGE INCIDENCE OF ATROPHY OF OLFACTORY NERVES IN MAN: A CONTRIBUTION TO THE STUDY OF THE PROCESS OF AGEING. CARLTON G. SMITH, J. Compt. Neurol. **77:** 589 (Dec.) 1942.

Smith examined 205 olfactory bulbs procured at autopsy from 121 persons of known age and sex who were free from intracranial disease. The ages ranged from birth to 91 years. By counting the number of olfactory glomeruli the author was able to estimate the number of fibers which reached a given bulb. The fibers began to disappear shortly after birth and continued to disappear at the rate of approximately 1 per cent a year. No sex difference in the loss of fibers was observed. Some subjects had entirely lost the olfactory fibers at the age of 20, and few had a normal count after the age of 50.

FRASER, Philadelphia

THE TROCHLEAR NERVE IN HUMAN FETUSES. ANTHONY A. PEARSON, J. Comp. Neurol. **78:**29 (Feb.) 1943.

The nucleus of the trochlear nerve in older human embryos and fetuses is a large mass of multipolar neurons located just caudal to the nucleus of the oculomotor nerve. The division between the trochlear and the oculomotor nucleus is indicated by a thinning out of the cells of the motor column. The trochlear nucleus consists of a main mass of cells, with an occasional smaller mass which lies farther caudad. The caudal group of cells may be bilateral or unilateral. When unilateral it is present on either the right or the left side, with equal frequency. A few cells of the type found in the mesencephalic root of the fifth nerve occur in the main nucleus of the trochlear nerve. In some embryos scattered cells are observed along the course of the trochlear nerve central to its decussation. These cells resemble neuroblasts. The fibers of the trochlear nerve are collected into several small bundles along the dorsolateral border of the trochlear nucleus toward its caudal end. All trochlear fibers appear to decussate. The trigeminal nerve contributes a small bundle of fibers which course with the trochlear nerve along its peripheral path and become lost in the meninges.

ADDISON, Philadelphia.

LIPOFUSCIN DISTRIBUTION IN THE BASAL GANGLIA. RUDOLPH ALTSCHUL, J. Comp. Neurol. **78:**45 (Feb.) 1943.

Altschul stained the basal ganglia of 2 children aged 3 months and 3 years respectively and of adults ranging in age from 42 to 84 years. He used a variety of stains to show the distribution of lipofuscin in nerve cells and neuroglia. The amount of lipofuscin in neuroglia cells of the basal ganglia was very small. The pigment was not a regular constituent of aging cells, but it occurred regularly in some of the cell systems. The nerve cells of the globus pallidus, the reticulate zone of the substantia nigra, the substantia innominata and the corpus subthalamicum were distinguished by the appearance and histochemical reaction of their lipofuscin. The nerve cells of the putamen and of the caudate and amygdaloid nuclei showed less typical reactions. Altschul believes that by the use of iron hematoxylin and basic fuchsin the lipofuscin present in the muscle of the human heart can be differentiated from the yellow pigment of nerve cells.

ADDISON, Philadelphia.

FUNCTIONAL RESULTS OF CROSSING SENSORY NERVES IN THE RAT. R. W. SPERRY, J. Comp. Neurol. **78:**59 (Feb.) 1943.

In three stages Sperry crossed the nerves which mediate cutaneous and deep sensibility of the left hindfoot so that they innervated the right hindfoot. The first stage of the operation was performed on rats from 14 to 26 days of age. The second and third stages were delayed until the nerves previously crossed had regenerated. In a later series of operations the completely denervated left foot was amputated at the second stage. In a number of animals in which the nerves had been crossed, the left saphenous nerve was kept intact and about 1 cm. of the right saphenous nerve was excised. The animals were tested for signs of recovery by placing them on a platform with a floor of cloth, through which the plantar surface of

the foot could be stimulated. The first signs of recovery appeared about forty-eight days after the first operation. About sixty days after the left saphenous nerve had been crossed (stage 2) cutaneous sensitivity began to reappear on the dorsal surface of the foot. In all animals there were false localization of sensation and a decided maladaptive reversal of the reflexes of the hindlimb. Despite prolonged training under various conditions, the maladaptive spinal reflexes remained in every case wholly uncorrected, or even inhibited by adjustment in the central nervous system.

ADDISON, Philadelphia.

THE DEVELOPMENTAL CONTROL OF PARS INTERMEDIA BY BRAIN. WILLIAM ETKIN, J. Exper. Zool. **92**:31 (Feb.) 1943.

In embryos of Rana pipiens, pituitary primordia, with and without varying amounts of neighboring brain tissue, were transplanted into young hypophysectomized animals. It was found that primordia developing in isolation from brain tissue induce excessive pigmentation in the host and show histologic evidence of overgrowth and hyperactivity. Primordia developing in contact with brain tissue at regions other than the infundibular floor behave as do isolated primordia. On the other hand, primordia developing in contact with the floor of the graft infundibulum at or near the normal point of attachment develop normally and show no evidence of excess function or growth. In grafts of the last type diencephalon with varying amounts of adjacent tissue was present. Grafts that do not take successfully may induce approximately normal pigmentation in the host.

These results seem to support the previously developed thesis that control of activity and growth of the pars intermedia is normally effected by inhibitory impulses brought to the gland over the hypothalamohypophysial nerve tracts. The effectiveness of control by an isolated section of brain indicates that the mechanism is not purely reflexive.

REID, Boston.

EXPERIMENTAL STUDIES ON THE DEVELOPMENT OF THE CORNEAL REFLEX IN AMPHIBIA: III. THE INFLUENCE OF THE PERIPHERY UPON THE REFLEX CENTER. JERRY J. KOLLROS, J. Exper. Zool. **92**:121 (March) 1943.

In Amblystoma (several species) and Triturus torosus the presence of a supernumerary eye in the otic area of the head modifies the response elicitable from that area. Stimulation of the extra cornea results in a retraction of the host eye on the same side instead of a head flexure (Triturus).

In Triturus, Amblystoma and Rana pipiens there is an increase in the sensitivity to tactile stimuli of the skin lying between the host and the graft eyes. In Triturus, and probably in Amblystoma, the influence of the graft is exerted throughout the larval period and beyond metamorphosis. The shrinkage of the reflexogenous area after metamorphosis (Triturus) is prevented, and there is an increase in local sensitivity. In Amblystoma and Rana the sensitivity of the graft also increases after metamorphosis.

Reduction in extent of the host cornea fails to reduce the extent of the reflexogenous area. Only the area of the replaced cornea itself has a lower sensitivity.

The cornea need not be completely differentiated to permit modulation of the sensory nerve fibers entering it.

REID, Boston.

Physiology and Biochemistry

EXPERIMENTAL RIBOFLAVIN DEFICIENCY IN MAN. JOHN J. BOEHRER, CHARLES E. STANFORD and ELIZABETH RYAN, Am. J. M. Sc. **205**: 544 (April) 1943.

The authors chose 6 volunteers, 1 man and 5 women, who previously had had dietary treatment for obesity. The subjects were divided into two groups of 3 each, designated as the "control" and the "experimental" group. The experimental, low riboflavin diet contained 471 mg. of riboflavin. All 6 patients received a daily supplement of vitamins and minerals, and the controls received, without their knowledge, a daily supplement of 3 mg. of riboflavin. The experiment was terminated after only five weeks of observation because of external circumstances. Each volunteer reported for study with the slit lamp. The failure of corneal vascularization to develop was not in accordance with the reported observations of Sydenstricker, Kelly and Weaver. It was significant that definite evidence of corneal vascularization occurred in 1 of the subjects of the control group, in spite of an intake of riboflavin of approximately 3.5 mg. per day, whereas an intake of approximately 2.1 mg. of riboflavin per day for seventy-nine days previously, while the subject was on the reduction diet, had not resulted in keratitis.

MICHAELS, Martinsburg, W. Va.

THE EFFECT OF SECTIONING VARIOUS AUTONOMIC NERVES UPON THE RATE OF EMPTYING OF THE BILIARY TRACT IN THE CAT. FRANK E. JOHNSON and EWARD A. BOYDEN, Surg., Gynec. & Obst. **76**:395, 1943.

The specific pathways to the choledochoduodenal junction, namely, the gastroduodenal nerve and plexus, were interrupted in cats. In one group of animals only the plexus was sectioned; in these cats the rate of emptying of the gallbladder following the ingestion of food appeared normal. But when the gastroduodenal nerve was cut in addition to the fibers of the plexus, decided retardation in the rate of emptying was observed. These observations were believed to indicate that the gastroduodenal nerve carries fibers which lower the resistance at the biliary outlet. Therefore the severance of nerves to the choledochoduodenal junction in patients should not be expected to lower the resistance to the flow of bile, but rather should increase it. The severance of the gastroduodenal nerve or plexus or both failed to affect or to abolish the inhibitory reflex to the gallbladder on electrical stimulation of the cecum. This result, therefore, appears to prove that stoppage of flow of bile from the gallbladder, as a result of visceral pain, is not dependent on action of the sphincter, since the tonus of the gallbladder can be inhibited in the absence of nerves to the choledochoduodenal junction.

Section of the right vagus nerve, which gives the only vagal component to the gastroduodenal nerve, resulted not only in increased resistance to the flow of bile at the sphincter but in decreased contractile force applied by the gallbladder, for the rate of emptying was much slower when the right vagus nerve was cut than when only the gastroduodenal nerve was eliminated. Section of the left vagus nerve also retarded the emptying of the gallbladder, but to a lesser degree than did section of the right vagus nerve.

Severance of the splanchnic roots of the celiac ganglia as far down as the second lumbar nerve abolished the inhibitory reflex from cecum to gallbladder and resulted in a somewhat accelerated rate of emptying of the gallbladder. Since section of the nerve to the sphincter (gastroduodenal nerve) retarded the flow of bile, the inference is that this nerve does not carry sympathetic inhibitory fibers. The retardation obtained by section of the vagus nerves was much greater than the acceleration caused by section of the splanchnic fibers.

When both the major and the minor splanchnic nerves were cut but the least splanchnic nerve was spared, the inhibitory reflex to the gallbladder was abolished, but the perception of pain on electric stimulation of the cecum persisted. This implies that pain impulses from the cecum enter the spinal cord as low as the second lumbar sympathetic ganglion, having traversed the superior mesenteric plexus and the least splanchnic nerve. SHENKIN, Philadelphia.

DISCHARGES FROM VESTIBULAR RECEPTORS IN THE CAT. E. D. ADRIAN, J. Physiol. **101**:389, 1943.

Nerve impulses from vestibular receptors were studied in the cat by means of oscillographic records obtained by insertion of fine wire electrodes into the brain stem in the region of the vestibular nuclei. Two main types of discharges from single units were observed, one controlled by gravity and the other by rotation. The former were found to depend on the position of the head in space; the latter, only on angular accelerations or decelerations. Discharges controlled by horizontal rotation and by the tilt of the head in the median plane were found near the oral border of the striae acusticae. Those controlled by lateral tilt and by rotation in the transverse plane were near the aboral border. Responses to vibration, such as have been reported in frogs, were not observed in cats.

The gravity receptors were increasingly stimulated as the head was tilted out of its normal position and became slowly adapted to the stimulus. They reacted to linear accelerations, as well as to the pull of gravity.

The rotation receptors were stimulated by angular acceleration in the horizontal, median or transverse plane or by deceleration of steady rotation in the nonstimulating sense.

The quick turns of the head were signaled by brief discharges which coincided with the movement, but acceleration not followed at once by deceleration gave discharges lasting up to twenty-five seconds. Equally long after-discharges followed deceleration from steady rotation in the nonstimulating sense.

The majority, but not all, of the rotation receptors gave persistent low frequency discharges when the head was at rest. These were suppressed by acceleration in the nonstimulating sense. The results support the view advanced by Ross that the receptors of the canals adapt slowly, the stimulus being proportional to the deflexion of the cupola. With a brief turn the reversal of the endolymph flow brings the cupola back at once to the mid-

position; with continued rotation the deflected cupola is brought back slowly by elastic forces and is then deflected in the other direction when rotation is stopped.

THOMAS, Philadelphia.

THE NEUROPHYSIOLOGY OF THE PARKINSON TREMOR. M. W. THORNER, Confinia neurol. **5**:113, 1942.

Thorner investigated the tremor of Parkinson's disease by means of electromyography. He expresses the belief that the tremor is a complicated form of oscillatory activity involving neural, muscular and mechanical components, which occurs as a result of the release of the normal damping effect of the basal ganglia. There is reciprocal and alternating contraction of antagonistic muscles. The frequency of the oscillation decreases as friction of the oscillating system increases and as the mass of the tremulous part is increased. A "feed back" mechanism is required for maintenance of the amplitude of the tremor. This is contained in part in the afferent return from the muscles involved and in part in the motor pathways of the central nervous system.

DEJONG, Ann Arbor, Mich.

MOVEMENTS OF LOCOMOTION IN THE DECEREBRATE CAT. CARLOS GUTIÉRREZ-NORIEGA, Rev. de neuro-psiquiat. **4**:333 (Sept.) 1941.

This is a physiologic study of locomotion by a pharmacologic method whereby all motor areas can be stimulated simultaneously with equal intensity. If locomotion were controlled from a limited area, the electrical method would be superior to the pharmacologic method, but since it is more probable that locomotion is an integrated action of many centers of the neuraxis, the pharmacologic method is preferable.

The procedure for study consisted of decerebration of the animal at the desired level, sufficient time being allowed for recovery from the effect of trauma; careful examination was made of all reactions of the animal (reflexes, tone, and movements of deambulation, spontaneous or provoked by electrical or mechanical stimulation); finally, nikethamide was injected into the saphenous vein, and the intensity and duration of the reaction were noted.

The following types of decerebrate cats were studied: bulbar, in which the transverse section was between the protuberance and the pons Varolii; hemiprotuberance, with the transverse section at the midpoint of the protuberance; protuberance, with the transverse section between the mesencephalon and the protuberance; hemimesencephalic, with the section in a transverse plane passing between the superior and inferior corpora quadrigemina posteriorly and the middle of the cerebral peduncules anteriorly; mesencephalic, with the plane of section from the superior border of the superior quadrigeminal bodies to the superior part of the mamillary bodies, and, finally, thalamic.

The term deambulation is used to indicate a complete function which permits each animal to displace itself in space and is integrated at least by the following elemental movements: rhythmic movements of flexion and extension of the extremities, which may also be called movements of progression or of deambulation; postural tone, in this case the tone of progression, and equilibrium. Only the movements of deambulation, which need not be confused with deambulation in general, are discussed.

Nikethamide was found to be the best stimulus in producing movements of deambulation. A specific center for locomotor function could not be isolated, for in the cat and dog an extensive region from the basal ganglia to the bulb takes part in this function. With the technic of progressive removal of the neuraxis, it was found that the magnitude of the disturbance of locomotor function produced by a lesion was directly related to the quantity of neural tissue removed, especially tissue from the cerebral trunk and basal nuclei.

Combined surgical-pharmacologic study disclosed that thalamic and diencephalic animals retained an almost normal gait. In mesencephalic animals deambulation was imperfect, since they walked with the legs semiflexed and fell at the slightest obstacle. The hemimesencephalic animals lost the capacity to deambulate, but if stimulated with nikethamide they presented powerful movements of flexion and extension of the forelimbs similar to those of running. The protuberance animals had poorer and less lasting responses than hemimesencephalic preparations when stimulated with nikethamide or metrazol, but the movements were more vigorous and there was more definite participation of all four limbs than in the hemiprotuberance animals. The latter had weaker and less lasting movement, mainly of the forelimbs, and required a larger dose of the drugs for effect. The bulbar animals failed to produce rhythmic movements of deambulation in the forelimbs, but in rare instances weak alternate movements of flexion and extension could be obtained in one limb or in a pair of limbs.

Thus, the various factors which integrate deambulation disappear in a progressive manner according to the amount of destruction of cerebral trunk, from the basal nuclei to the bulb. Extirpation of the cerebellum failed to modify the effect of nikethamide on the movements of deambulation.

Gutiérrez-Noriega demonstrated that the zone between the basal ganglia and a plane which passes between the bulb and the protuberance is particularly concerned with movements of deambulation in the cat. Although it is certain that deambulation, strictly speaking, is found only in thalamic and diencephalic animals, the simple movements of deambulation of the extremities can originate from electrical, mechanical or pharmacologic stimuli to inferior parts of the neuraxis. Such movements can be obtained in animals in which only the inferior part of the protuberance is preserved. From this the author concludes that movements of deambulation cannot be localized in a specific center or in a limited group of centers. Even less so can locomotion be localized. It is certain that the efficiency of the act of progression diminishes proportionately with the amount of neural tissue removed.

The thalamic animal walks, but not as perfectly as the intact animal. If the thalamus is removed the stability, frequency and complexity of movements diminish. The mesencephalic animal walks defectively or, better, drags itself about with the legs semiflexed, but if it is put in dorsal decubitus it can move the four extremities perfectly with the same series of combinations of flexion and extension of the four limbs as is required in normal progression. Therefore, extirpation of the thalamus, including the hypothalamus, affects principally not the rhythmic movements of the extremities but the distribution of tone and of equilibrium necessary to maintain the animal erect during deambulation.

DE GUTIÉRREZ-MAHONEY, Coral Gables, Fla.

EXPERIMENTAL CATALEPSY PRODUCED BY NICOTINE. CARLOS GUTIERREZ-NORIEGA, Rev. de neuro-psiquiat. **5**:323, 1942.

Gutierrez-Noriega studied the cataleptic action of nicotine in dogs. One hundred animals were divided into five groups of 20 each, each group receiving a different dose of nicotine tartrate, varying from 1 to 5 mg. per kilogram of body weight. The drug was injected into the saphenous vein in a 1 per cent solution. The intensity of the cataleptic state was measured by the duration of abnormal postures. Three observations were made: (1) the average frequency of occurrence of the cataleptic state in each group; (2) the average intensity, and (3) the average duration. From the data he obtained a "cataleptic index"—one-tenth the sum of the three values. Observations were also made on the severity of the convulsions and their relation to the intensity of the catalepsy. The results obtained indicated that nicotine tartrate can cause reactions of cataleptic type, as well as other manifestations of experimental catatonia, such as motor excitation, neurovegetative changes and lack of response to painful stimuli. The doses that produce these reactions are also convulsant, but the catalepsy may appear independently of convulsions. In fact, the optimum dose for production of catalepsy (3 mg. per kilogram) is not the optimum dose for production of convulsions.

Although there is a correlation between the dose and the intensity of the cataleptic reaction, there is a still greater relation to the constitution of the animal, docile, quiet and friendly animals being more susceptible than active, impetuous and surly dogs. The author suggests that his method of obtaining a cataleptic index be used in study of the action of drugs of this type in large numbers of animals. Several graphs and charts illustrate the paper.

Meninges and Blood Vessels

HEMIPLEGIA IN TUBERCULOUS MENINGITIS. CLARENCE W. OLSEN and ALBERT F. BROWN, Bull. Los Angeles Neurol. Soc. **7**:189 (Dec.) 1942.

Olsen and Brown report 4 cases of hemiplegia associated with tuberculous meningitis. The incidence of this complication in a series of 378 cases of tuberculous meningitis with both clinical and postmortem reports slightly exceeded 10 per cent. LESKO, Bridgeport, Conn.

RESPONSE OF PFEIFFER'S BACILLUS MENINGITIS TO SULPHAPYRIDINE. RAYMOND A. MOIR, Lancet **1**:556 (May 1) 1943.

Moir reports 4 cases of meningitis due to Haemophilus influenzae. In only 2 of these 4 cases did recovery occur. He believes that the bacilli were too scanty in the original smear of the cerebrospinal fluid for much credit to be attributed to the drug for the recovery in 1 of the 2 cases. Fothergill and Sweet (*J. Pediat.* **2**:696, 1933) reported only 1 spontaneous recovery in 78 cases. The other recovery in Moir's cases (that of a 10 month infant) he feels was a true cure, especially since children under 1 year of age have not been known to recover spontaneously.

In this series Moir noted that the temperature might drop to normal only to rise again, whereas the pulse stayed high until the temperature had fallen permanently. Hence the pulse is taken as a more reliable guide in prognosis than the temperature.

He recommends that lumbar puncture be done once for diagnosis, the procedure to be repeated only if restlessness and irritability become uncontrollable; otherwise, a second tap should not be done until the patient is clinically well.

Administration of sulfapyridine in doses of no less than 3 Gm. per twenty-four hours is advised with continuation of the drug in reduced doses for two weeks after meningitic signs are gone.

McCarter, Philadelphia.

Pneumococcal Meningitis: Recovery After Sulphapyridine and Serum Therapy. H. A. Thomas, R. J. Twort and C. P. Warren, Lancet **1**:581 (May 8) 1943.

The authors report a case of pneumococcic meningitis following mastoiditis. The patient was first treated with sulfapyridine but in a few days was also given type-specific anti-pneumococcic serum, since he was not improving under treatment with the drug alone. There was rapid change for the better after the first 100,000 units (U. S. P.) of the serum, a change so dramatic that the authors suggest it was more than coincidence and probably indicates that the serum was the chief curative factor. Several days after convalescence had begun sciatic neuritis with foot drop developed on the right side. Intramuscular injection of the sulfapyridine is offered as the most likely cause of this complication. In the sixth month after the illness developed the patient suddenly had a focal epileptic attack, followed by hemiparesis and motor aphasia, from which he slowly recovered.

McCarter, Philadelphia.

The Relationship Between Benign Lymphocytic Meningitis and Poliomyelitis. P. Gautier and G. Henny, Confinia neurol. **4**:309, 1942.

Gautier and Henny note certain similarities between lymphocytic choriomeningitis and poliomyelitis, namely, in the constituents of the spinal fluid, in the epidemiology and in the clinical course. They state that the two conditions often occur simultaneously. They express the belief that all cases of lymphocytic meningitis which run a benign course should be regarded as instances of an attenuated form of poliomyelitis or of poliomyelitis in which the disease process is limited to the meninges.

DeJong, Ann Arbor, Mich.

Thrombosis of the Common Carotid Artery. T. Fracassi, Semana méd. **49**:1004 (May 14) 1942.

Fracassi reports a case in which a clinical diagnosis of thrombosis of the common carotid artery with complete occlusion was made. No clinical diagnosis of this condition has previously been reported in the literature. In the case reported by Wohlwill, necropsy revealed syphilitic aortitis with thrombosis of the common carotid artery at the point of its origin. The communicating posterior artery of the opposite side was so greatly dilated that an adequate collateral circulation had been established to take care of the occluded side. Fracassi's patient, aged 58, had a chancre in his youth. The chancre disappeared without treatment. The patient at no time exhibited syphilitic, circulatory or nervous symptoms. At the examination it was found that he had suffered for about three months from intermittent attacks of local pallor and coldness of the right hand and foot. There was also an attack of apoplexy, with coma of ten hours' duration, transient aphasia and right hemiplegia. The patient complained of pulsation and pain in the region of the right temporal artery and its branches, which did not yield to analgesics. The heart was normal. The pulse was normal, with a maximum arterial pressure of 100 mm. The Wassermann reaction was positive. Bismuth and mercury therapy was administered. Three years later the patient was in a satisfactory state of health, with normal intelligence and normal speech. An aortic murmur was audible. The roentgenographic shadow of the aorta was widened. Electrocardiograms showed changes in the myocardium. The left common carotid artery and its internal and external branches and the left temporal, angular and facial arteries did not pulsate. The right common carotid artery and its branches pulsated strongly. The blood pressure in the right radial artery was 115 mm., while in the left it was 100 mm. The retinal vessels of the left eye were narrowed. There was normal pulsation in both pedal arteries. Right hemiplegia and deep and superficial anesthesia were present on the right side. A clinical diagnosis of thrombosis of the common carotid artery was made. The hemiplegia was caused by softening of the brain tissue in the region of the left sylvian artery. The dilatation and forced pulsation

of the right local arteries, on the one hand, and the narrowing of the left retinal vessels, on the other, confirmed the diagnosis. The author emphasizes the diagnostic significance of the absence of pulsation in the temporal and carotid arteries of one side and of forceful pulsation of the arteries of the opposite side in cases of hemiplegia, changes which indicate thrombosis of the primary common carotid artery.

J. A. M. A.

CHRONIC TUBERCULOUS CEREBROSPINAL LEPTOMENINGITIS. B. SCHMIDT, Beitr. z. Klin. d. Tuberk. **96**:124 (March 21) 1941.

Schmidt reports the case of a man aged 28 who, since the age of 18, had presented obscure cerebral symptoms with convulsions, loss of consciousness and mental disturbances. Necropsy disclosed chronic tuberculous cerebrospinal leptomeningitis with tubercles in the dura, internal hemorrhagic pachymeningitis, calcified foci in the tracheobronchial lymph nodes, inflammatory swelling and tuberculosis of the paratracheal and hilar lymph nodes of both lungs, pleural adhesions and catarrhal urocystitis with dilatation of the bladder, ureters and renal pelves. Microscopic examination of the lymph nodes disclosed calcified tuberculous foci. The microscopic aspects of the brain are described in detail. There was evidence that the chronic tuberculosis of the leptomeninges had a strong tendency to cicatrization. The author cites 3 similar cases from the literature.

J. A. M. A.

MENINGOCOCCIC MENINGITIS TREATED WITH SULFATHIAZOLE. H. PEDERSEN and J. WILKENSCHILDT, Ugesk. f. læger **103**:1562 (Dec. 4) 1941.

Because of its easier absorption and elimination and its less toxic by-effects, Pedersen and Wilkenschildt consider sulfathiazole superior to the other sulfonamide compounds previously used in the treatment of meningococcic meningitis. They report 11 cases in which this agent was employed, in 7 of which the condition was toxic, with cutaneous metastases. In all the cases meningococci were present in the spinal fluid. Nine of the patients recovered rapidly; 2 died, 1 a child aged 5 months and the other a man who was moribund on admission. The sulfathiazole was administered orally in tablet form except in the case of the 5 month old child, to whom it was given intramuscularly.

J. A. M. A.

Diseases of the Spinal Cord

ENCEPHALO-MYELO-RADICULITIS. CHARLES G. POLAN and A. B. BAKER, J. Nerv. & Ment. Dis. **96**:508 (Nov.) 1942

Polan and Baker report 8 cases of encephalomyeloradiculitis, calling attention to the diversity of terms under which the disease has been described. They regard the condition as a syndrome. In most cases the disease is preceded by an infection of the upper respiratory tract. Neurologic symptoms are sudden in onset and consist of muscular weakness or paralysis, distal hyperesthesias, radicular pain and aching muscles. The lower extremities, especially the distal parts, are more often involved early in the disease. Unilateral or bilateral weakness of the face is common. Objective signs are variable, but usually appear as ascending flaccid paresis or paralysis with diminished deep reflexes. Sensory disturbances follow a segmental or radicular distribution. The temperature and leukocyte counts are usually normal, or only slightly elevated. A high protein content of the spinal fluid with a normal cell count is characteristic of the disease, but it is not constant. Most patients begin to recover after an acute onset, but recovery is usually slow. Fatalities are infrequent and are usually due to complications or involvement of the medulla. Treatment is symptomatic and includes rest in bed, use of the Drinker respirator when necessary, small transfusions, administration of large doses of vitamins B and C, tidal irrigations of the bladder, administration of sulfonamide compounds in cases of involvement of the bladder and physical therapy for muscle disorders. Pathologic lesions vary with the extent and location of the disease process. In 1 case there were fairly extensive injury to the neurons of the cranial nerves and spinal cord and scattered areas ot local demyelination involving the gray and the white matter, most of it scattered around the blood vessels.

CHODOFF, Langley Field, Va.

TONSILLECTOMY AND POLIOMYELITIS. J. A. TOOMEY and C. E. KRILL, Ohio State M. J. **38**:653 (July) 1942.

Toomey and Krill tabulate the results of fourteen years' experience in the relation of poliomyelitis to tonsillectomy at the Children's Hospital in Akron, Ohio, and of one year's experience at the City Hospital of Cleveland. Seventeen of the 210 patients at the Children's

Hospital died, as did 18 of the 220 patients at the City Hospital. In 14, or 82 per cent, of 17 patients who had had a tonsillectomy or adenoidectomy within thirty days prior to the onset of poliomyelitis the bulbar type of paralysis developed. Of 134 patients operated on prior to thirty days before onset at both hospitals, 52 had bulbar poliomyelitis. Eight, or 50 per cent, of the 16 children with the bulbar type died. At the City Hospital 8 of the 36 died. In 7, or 5 per cent, of 140 nonsurgical patients admitted to the Children's Hospital and 23, or 19.4 per cent, of 118 similar patients admitted to the City Hospital bulbar poliomyelitis developed. Here, again, most of the children who died had the bulbar type—5 of the total 7 at the Children's Hospital and the 9 at the City Hospital. If only the mortality of the group that had spinal or nonparalytic poliomyelitis is considered, the rate seems insignificant —2 per cent at the Children's Hospital and none at the City Hospital. The many persons who had had tonsillectomy and adenoidectomy within thirty days of the development of bulbar poliomyelitis cannot be explained on the basis of mere chance or random sampling. In the regions discussed, it appears to be advisable to do tonsillectomies in the late spring.

J. A. M. A.

Cerebrospinal Fluid

THE CEREBROSPINAL FLUID. ROQUE GRAZIANO, Rev. argent. de neurol. y psiquiat. **7**:83 (June) 1942.

On the basis of a review of the anatomic relation, chemical composition, circulation, cytologic characteristics and diagnostic significance of the cerebrospinal fluid, Graziano concludes: 1. Studies of the cerebrospinal spaces at autopsy confirm the concept that the cerebrospinal fluid is formed by the choroid plexuses. 2. The cerebrospinal fluid varies in composition in different regions of the cerebrospinal spaces. 3. Analysis of the cerebrospinal fluid at various stages of the course of a disease enables one to determine the development of the malady, just as do the clinical symptoms. This is illustrated by the evolution in the number of lymphocytes and polymorphonuclear leukocytes in the course of pneumococcic meningitis. 4. The constellation of findings in the fluid, not its separate constituents, is important for diagnosis. 5. In diseases of the nervous system caused by Treponema pallidum the constellation of findings in the fluid differs from that in other diseases.

BAILEY, Chicago.

Treatment, Neurosurgery

NON-CONVULSIVE ELECTRIC (FARADIC) SHOCK THERAPY OF PSYCHOSES ASSOCIATED WITH ALCOHOLISM, DRUG INTOXICATION AND SYPHILIS. NATHANIEL J. BERKWITZ, Am. J. Psychiat. **99**: 364 (Nov.) 1942.

Berkwitz reports the results of nonconvulsive electric shock treatment of 67 patients with alcohol and drug addiction and of 5 patients with dementia paralytica. This treatment was given in addition to the generally accepted therapeutic regimens. Most patients showed improvement with one to four treatments; only rarely was it necessary to administer more than ten shocks. Improvement manifested itself chiefly by decrease in the period of delirium.

FORSTER, Philadelphia.

SUBCONVULSIVE ELECTRIC SHOCK TREATMENT OF THE PSYCHOSES. WALTER A. THOMPSON, Am. J. Psychiat. **99**: 382 (Nov.) 1942.

Thompson reports on the use of subconvulsive electric shock therapy with 213 patients. The shocks were induced by a faradic current of high voltage and low amperage passed between the head and the leg electrode. The result was a tetanus-like convulsion without loss of consciousness. No particular group of patients was studied, the conditions of the patients representing all types of psychoses available. No cures were obtained, but 65 per cent of the series showed some improvement in hospital adjustment.

FORSTER, Philadelphia.

THE TREATMENT OF PSYCHOSES WITH LONG PROTRACTED INSULIN COMA. JOSEPH WORTIS, MILTON TERRIS and IRVIN M. KORR, Am. J. Psychiat. **99**: 391 (Nov.) 1942.

Wortis, Terris and Korr have succeeded in prolonging hypoglycemia for twenty-four hours and coma for twenty hours by maintaining the blood sugar at a moderately high level (35 mg. per hundred cubic centimeters). Irreversible coma could be prevented by careful attention to the blood sugar level, the pulse rate, the temperature and the patient's general condition.

Caution in the general application of this form of therapy is recommended. The authors have no adequate statistics on the therapeutic value of this treatment but indicate that it may be more advantageous than the usual insulin therapy.

FORSTER, Philadelphia.

EVALUATION OF THE EFFECTS OF INTRAVENOUS INSULIN TECHNIQUE IN THE TREATMENT OF MENTAL DISEASES. PHILLIP POLATIN and HYMAN SPOTNITZ, Am. J. Psychiat. **99**:394 (Nov.) 1942.

Polatin and Spotnitz report the results of insulin shock therapy induced by intravenous administration of insulin or protamine zinc insulin crystals. The protamine zinc insulin preparation was used when patients were allergic to unmodified insulin. The authors treated 33 patients, 24 of whom were schizophrenic. Definite improvement occurred in 14 patients, 4 of whom had a relapse within two years. The authors believe that the intravenous administration of insulin for induction of shock is the method of choice for patients with psychoses of acute onset and short duration.

FORSTER, Philadelphia.

PREFRONTAL LOBOTOMY IN CHRONIC PSYCHOSES. MAGNUS C. PETERSEN and HAROLD F. BUCHSTEIN, Am. J. Psychiat. **99**: 426 (Nov.) 1942.

Petersen and Buchstein studied 46 patients who had undergone prefrontal lobotomy for long-standing psychoses. Psychic tension was the criterion for operation. No patient died as a direct result of the operation, but 1 patient died eleven days after operation of pharyngeal obstruction due to her failure to swallow food. The importance of this situation is stressed. Flushing and sweating occurred immediately after the section of cerebral tissue, and in some instances conjugate ocular deviation and a positive Babinski sign were noted. Bradycardia and hypotension occurred constantly, the bradycardia being of longer duration than the hypotension. Most of the patients had increased appetite after the operation, and 13 showed increased dextrose tolerance. Almost all the patients manifested untidiness. The most striking phenomenon was relief from tension immediately on bilateral section. Sixteen of the authors' 29 patients who were operated on in 1941 showed improvement. FORSTER, Philadelphia.

ELECTRIC SHOCK TREATMENT IN GENERAL PARESIS. GERT HEILBRUNN and PAUL FELDMAN, Am. J. Psychiat. **99**:702 (March) 1943.

Heilbrunn and Feldman administered from two to seven electric shock treatments to each of 5 patients with dementia paralytica. No improvement in the clinical condition was noted. However, therapy had to be discontinued because of the development of alarming cardiovascular and respiratory complications. These were attributed to the heightened vulnerability of the ganglion cells in neurosyphilis. Heilbrunn and Feldman conclude that electric shock therapy is a perilous therapeutic procedure for dementia paralytica.

FORSTER, Philadelphia.

ON THE USE OF STRYCHNINE IN THE CURARE-AIDED METRAZOL TREATMENT OF PSYCHOSES. MARCEL HEIMAN, Am. J. Psychiat. **99**:706 (March) 1943.

Heiman administered simultaneously strychnine and curare to 30 female patients with psychoses and followed this with metrazol. He found that strychnine reduced the metrazol requirement and had a beneficial influence on respiration, its action thus tending to offset the central effect of metrazol and the peripheral effect of curare. FORSTER, Philadelphia.

EXTRA-MURAL SHOCK THERAPY. LOUIS WENDER, BENJAMIN H. BALSER and DAVID BERES, Am. J. Psychiat. **99**: 712 (March) 1943.

Wender, Balser and Beres treated with electric shock 40 patients from the office and outpatient department, 31 of whom had major psychoses. The authors consider the patient's refusal to be hospitalized or the physician's opinion that it is not advisable as indications for extramural therapy. The technic differed in no way from the intramural method. The average duration of therapy was five weeks. There were 6 failures in the entire series. The authors conclude that the results are comparable to those obtained with hospitalized patients. The importance of follow-up psychotherapy is stressed. FORSTER, Philadelphia.

VITAMIN B THERAPY IN PARALYSIS AGITANS. WINIFRED C. LOUGHLIN, H. ARNOLD MYERSBURG and HERMAN WORTIS, Ann. Int. Med. **17:** 423 (Sept.) 1942.

Twenty-two unselected patients with paralysis agitans were used as subjects in a determination of the effects of vitamin B therapy. The ages ranged from 28 to 72 years, the average age being 49.2 years. The duration of symptoms varied from three to thirty-three years. The patients were divided into two groups; a group of 12 patients received daily intravenous doses of vitamins, while the other group, of 10 patients, received daily injections of 5 cc. of isotonic solution of sodium chloride. All the patients continued to have whatever other therapy they were receiving prior to the onset of the experiment. Examinations were made at weekly intervals during the experiment. The vitamin-treated patients received intravenous injections of a preparation containing 10 mg. of thiamine hydrochloride, 10 mg. of nicotinamide, 1 mg. of riboflavin, 10 mg. of pyridoxine hydrochloride and a buffered solvent up to 5 cc. Each patient received six intravenous injections each week for five and one-half weeks, and for the next five weeks the same number of injections weekly, with the addition of 90 mg. of pyridoxine hydrochloride. The controls received daily injections of 5 cc. of sterile isotonic solution of sodium chloride for ten and one-half weeks.

There was no objective improvement in the vitamin-treated group. Two patients in the group reported subjective improvement. Of the control group, 9 showed initial subjective improvement, in 3 of whom it persisted throughout the treatment. One of the patients, of the control group, showed objective improvement.

PRICE, Philadelphia.

THE TREATMENT OF ESSENTIAL HYPERTENSION BY SYMPATHECTOMY. JAMES BORDLEY III, MORTON GLADSTON and WALTER E. DANDY, Bull. Johns Hopkins Hosp. **72:** 127 (March) 1943.

The presence of incapacitating symptoms was the only criterion for sympathectomy in 12 patients with essential hypertension. Ten of the patients were from 28 to 40 years and 2 were 50 years of age at the time of operation. In 3 patients a supradiaphragmatic splanchnicectomy (Peet operation), and in 9 patients an infradiaphragmatic splanchnicectomy (Adson-Craig operation), was performed. The level of the arterial pressure was lower for six to eighteen months in 4 of the 9 patients treated by infradiaphragmatic operation. Symptomatic relief, obtained in 4 patients, seemed to depend on lowered arterial pressure. In 2 patients on whom the infradiaphragmatic (Adson-Craig) operation was performed the abnormal signs referable to the heart and eyegrounds regressed during the period of lowered arterial pressure but returned with elevation of the pressure. The return of the arterial pressure to hypertensive levels was not accompanied by regeneration of the sympathetic nerves to the lower extremities after the Adson-Craig operation. The group of patients was not large enough to warrant the formation of conclusions concerning the relative incidence of reduction in the level of arterial pressure following sympathectomy in patients with changes in the eyegrounds, of various degrees of severity.

PRICE, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

ARTHUR WEIL, M.D., *President, in the Chair*

Regular Meeting, April 15, 1943

Plastic Repair of Defects of the Skull. DR. HAROLD C. VORIS.

Materials available for the repair of defects of the skull may be divided into three general groups: living autogenous bone or cartilage; boiled or preserved bone or cartilage, and alloplastic materials, of which pyroxylin and various metals have been the most popular. Living bone or cartilage may be obtained from various parts of the patient's body, but the two most common sources are the ribs or costal cartilages and the periosteum and attached fragments of the outer table of the skull. Rib or portions of the skull can be obtained from other persons or from cadavers and can be sterilized by boiling before insertion. The greatest use, however, for such grafts is the replacement of areas of skull invaded by tumor cells, after such areas have been temporarily removed and boiled.

Pyroxylin has been widely used in the past, as well as many metals, particularly silver, gold and aluminum. The recent investigations of Venable, Campbell, Pudenz and others have shown that certain alloys and metals are noncytotoxic; of these, vitallium, tantalum and ticonium (wrought) appear to be the best.

Cases are presented, with lantern slides from these and other cases, illustrating the replacement of bone flaps after boiling, plastic repair with rib or rib cartilage, employment of grafts consisting of periosteum and the outer table of the skull and, finally, use of the vitallium plate.

Repair of defects of the skull is indicated (1) for cosmetic reasons; (2) for protection, when the occupation renders the patient particularly liable to head trauma; (3) for severe subjective symptoms, such as headache, dizziness and pain in the region of the defect; (4) for undue pulsation of the scalp overlying the defect; (5) for economic reasons, when the patient is unable to obtain a position because of the presence of a defect in the skull, and (6) for relief of an unfavorable psychic effect. All defects of the frontal region below the hair line, including those of the supraorbital ridge, should be repaired. Small defects within the hair line seldom need repair; large defects within the hair line which fall into one of the classes just indicated may be repaired. A graft consisting of periosteum and attached fragments of the outer table of the skull is the most satisfactory for small defects. The use of rib or costal cartilage is advised for defects of the supraorbital ridge; for larger defects of the skull employment of one of the noncytotoxic alloys or metals is suggested.

DISCUSSION

DR. ERIC OLDBERG: Dr. Voris is to be complimented on the satisfactory cosmetic results he has shown. I should like to emphasize that the patient with a defect in the skull is much safer in the hands of a neurosurgeon than he would be in the hands of a plastic surgeon, whose knowledge of intracranial problems is necessarily limited. In work like Dr. Voris' there are invariably problems, such as those concerned with defects in the dura and choice of time following infection, which require specialized knowledge.

Bilateral Prefrontal Lobotomy: Perspective and Recent Survey of Results. DR. LLOYD H. ZIEGLER, Wauwatosa, Wis.

Historically, the so-called drastic therapies of the psychoses are not new. Paracelsus gave camphor to induce convulsions; Benjamin Rush offered the tranquilizer. Malarial therapy appeared, and then, in rapid succession, insulin, metrazol and electric shock therapies. These methods of treatment tended to interest physicians in the functions of the brain, especially of the frontal lobe. All this has led to the operation of prefrontal lobotomy. A recent survey of the results of this operation in various clinics in this country and in Canada is summarized in the accompanying table.

Survey of Results of Bilateral Prefrontal Lobotomy Reported from Seventeen Clinics in the United States and Canada (January to March 1943) on Patients with a Variety of Psychiatric Reaction Types, Schizophrenia Predominating

No. of patients operated on	582
Deaths resulting from operation	11
Deaths subsequent to operation	16*
Patients rendered clinically worse by operation	8
Patients with no clinical improvement after operation	60
Patients with slight clinical improvement after operation	111
Patients showing much clinical improvement after operation	192
Patients recovered after operation; psychotic or neurotic symptoms disappeared	184
No. of patients known to be in hospital at time of study (some able to work)	265
Patients known to be outside hospital but unable to work	55
Patients known to be outside hospital, working part or full time	235

* One patient committed suicide.

As in the case of shock therapy, the first reports are usually more optimistic than they should be. Prefrontal lobotomy is a new therapeutic endeavor, and the results must be followed closely for a number of years before the permanency of the reported ameliorations can be evaluated and the types of patients most likely to be benefited can be determined.

DISCUSSION

DR. HOWARD ZEITLIN: At the Neuropsychiatric Institute, under the direction of Dr. Francis Gerty and Dr. Eric Oldberg, my associates and I undertook a study of psychiatric patients on whom lobotomies had been performed. This project entailed the study by various psychologic methods of changes in the frontal lobe following the operation. Through Dr. Percival Bailey, we have had the opportunity to operate on 5 patients since September 1942. The number was restricted to suitable patients: First, patients showing moderate degrees of mental deterioration were excluded, and, second, lobotomy was performed only after more conservative measures, such as psychotherapy and electric shock and insulin therapy, had failed to maintain improvement in the disturbed personality. Preoperative and postoperative studies were made. Special tests for function of the frontal lobe were carried out by Dr. Ward Halstead.

The first patient, with hebephrenic schizophrenia and some degree of deterioration, although not presenting the ideal conditions for operation, had a lobotomy because of the family's desire that it be tried. He has

since returned home. Although he is not yet working, he has been able to adjust, but at a lower level.

Another patient had paranoid schizophrenia, or what was thought by some examiners to be paranoia, with a fixed system of delusional ideas. For about three months after operation he improved notably. Although his paranoid ideas were still present, they remained in the background, and he no longer talked about them. On his return home, he went back to work for about a month. Recently his paranoid ideas have returned, and he is again preoccupied with them. He is being seen in the outpatient clinic each week.

The best therapeutic result was obtained in a patient whose mental illness was motivated by outstanding anxiety. Early in his life he had a psychotic episode of short duration. Reactive depressive states were frequent prior to operation. They had improved with electric shock therapy and, later, with insulin treatment, but after each course, with the return of anxiety, he failed to maintain his improvement. In the interval between episodes he displayed pronounced hypochondriacal symptoms, which finally passed into an obsessive, ruminative state, during which he spent most of the day thinking about himself. His anxiety would mount in intensity until he again passed into a depressive state. During the latter state self-destructive impulses were manifested. He tried suicide, and prior to operation he made a combined homicidal and suicidal attempt. At a conference of the entire staff the opinion was expressed that the prognosis was poor.

Almost immediately after operation the patient lost all his anxiety, as well as his hypochondriacal complaints. He is now working in a defense plant. He is fairly well adjusted and is getting along well. It is my opinion that a patient of this type is ideal for lobotomy.

Of the 5 patients operated on, 1 died of postoperative hemorrhage. However, we feel that the mortality rate should not run higher than that after operation for uncomplicated appendicitis.

It is obvious that lobotomy is not a cure-all for mental illness, but we feel it has a place in the treatment of mental disorders. So far as can be determined from our limited number of patients, it eradicates anxiety completely. This does not mean, however, that there is complete loss of the "worry center" or that the patient is reduced to a vegetative existence. Actually the personality does not change much from that prior to operation except for the changes that may be expected with the loss of anxiety. Furthermore, lobotomy does not interfere with the later use of extensive psychotherapy or psychoanalysis. In fact, the procedure makes possible psychoanalysis in cases in which the illness was formerly refractory to such therapy.

A complete report of our cases will be made later.

DR. WARD HALSTEAD: Through the courtesy of Dr. Zeitlin, I have examined on several occasions the patient whom he described as presenting a perfect result of lobotomy. I first examined the man after operation. I agree that he presents a striking picture of apparent "normality." If the patient were here this evening I should challenge any one to pick him out of this group on the basis of his general behavior. His performance on a wide range of psychologic tests of the paper and pencil type falls well within normal limits. My category test, however, revealed both quantitative and qualitative evidence of a severe underlying pathologic state. Marked constriction of the dynamic visual field was also noted. I am continuing my study of this patient, and I prefer to postpone further comment until I am in a position to make a more complete presentation of the results.

With regard to Dr. Zeitlin's comment that the amount of intellectual impairment following lobotomy is not as great as might be expected, I can only take exception to the methods which have thus far been brought to bear on this important question.

DR. A. EARL WALKER: I should like to add a word of caution. I am not sure that it is a good thing to turn a patient out into society without "worry centers." One should know more about the precise mental faculties of patients following prefrontal lobotomy before endorsing this procedure for the mentally ill. I doubt whether such persons will be able to carry on normally in society. It is quite true that a considerable number, as Dr. Ziegler has pointed out, have been able to return to some form of work, but it is a quite different matter for a patient to do work under supervision than for him to return to his usual occupation and carry it on successfully. Few patients have been able to do that.

DR. CONRAD S. SOMMER: Was any attempt made to evaluate the role of other methods of treatment, such as occupational therapy or psychotherapy, in producing the results attributed to the operation?

DR. LLOYD ZIEGLER, Wauwatosa, Wis.: Dr. Halstead has answered a question I was about to ask; Dr. Zeitlin's patient may have been immature and would have shown it if tests had been made prior to operation.

I agree with Dr. Walker about worry. It is a sign of illness to lose all capacity to worry. Of course, an excess of it annihilates the useful functions of a person, also.

In answer to Dr. Sommer's question, I have relatively little information on the adjunctive therapies that were administered to these patients. Some had been given all forms of shock therapy; some had had none. Some were subjected to psychotherapy before and after the operation; some were given shock therapy after operation and improved. From the reports that came to me I could not always tell with certainty to what reaction type the patient belonged. For that reason, I made no attempt to classify these patients.

The Diagnostic Value of Electroencephalography.

DR. VASILIOS S. LAMBROS, DR. THEODORE J. CASE and DR. A. EARL WALKER.

Electroencephalography is an important and valuable aid in the diagnosis of the convulsive state and of intracranial tumors, giving evidence of alterations in the electrical activity of the brain in a large percentage of cases. Roentgenography of the skull, on the other hand, rarely shows abnormalities associated with the convulsive state. It is suggested therefore that electroencephalography, rather than roentgenography of the skull, be used as a routine procedure in the diagnosis of the convulsive state.

In cases of intracranial tumor the percentage of localizing alterations in the electroencephalogram is approximately 50, an incidence which is greater than that for alterations in roentgenograms of the skull. Moreover, localizing phenomena are present in cases in which there are no clinical localizing signs. Electroencephalography should be a routine procedure in every case in which an intracranial tumor is suspected.

DISCUSSION

DR. CHESTER W. DARROW: I wish to congratulate the authors on their presentation of a paper which contributes to the clinical usefulness of the electroencephalogram. Was evaluation of the data based on records which included the effects of hyperventilation, and, if so, was this procedure considered necessary?

DR. PERCIVAL BAILEY: Did the electroencephalogram lead to an erroneous localization in any case?

DR. RICHARD B. RICHTER: It is gratifying to have such a statistical analysis of the value of electroencephalography. But to me these figures spell something rather different than the authors have seen in them, at least with reference to the convulsive state in general. It should be noted that the cases were selected because of a clinical history of epilepsy. In 75 per cent there were electroencephalographic abnormalities. I should like to know whether, on this account, a diagnosis of epilepsy in the broad sense of the term was excluded in the remaining 25 per cent or in any considerable proportion of this series. If not, it is difficult to see that the electroencephalogram was of real diagnostic value. Furthermore, there was no significant difference in the proportion of abnormal tracings in the cases of the organic and in the cases of the nonorganic type; when such changes did appear in cases of organic origin they were seldom qualitatively distinctive or of localizing value.

DR. VASILIOS S. LAMBROS: In answer to Dr. Darrow, all these tracings were taken with the patient breathing normally. At this time my associates and I did not employ hyperventilation.

In reply to Dr. Bailey, the electroencephalogram led to wrong localization in 3 cases; however, in all 3 of these cases there was an extensive infiltrating glioma. These 3 cases were included with the group in which positive electroencephalographic features were present but the lesion was not localized.

DR. A. EARL WALKER: Dr. Richter has presented an interesting paradox. However, I do not believe that a method of examination should be said to be of no value because it does not always enable one to make a diagnosis. Nor should the diagnosis be altered in any way because the method does not point to the diagnosis.

In many cases of tumor of the brain an electroencephalogram will present valuable evidence, but that the electroencephalogram is normal does not imply that the brain is not the site of neoplastic invasion. The same principle applies in the diagnosis of a convulsive state. In the great majority of cases of convulsive seizures the brain waves are abnormal, but in a certain number no abnormality is present; yet the diagnosis of epilepsy must be made on the basis of the clinical history.

PHILADELPHIA PSYCHIATRIC SOCIETY

HAROLD D. PALMER, M.D., *President, in the Chair*

Regular Meeting, May 21, 1943

Further Statistics on Electric Shock Therapy. DR. THOMAS WRIGHT JR.

In the past year my associates and I at the Pennsylvania Hospital for Mental and Nervous Diseases have treated 117 patients with electric shock. To these 117 patients we gave 1,006 treatments. Each person received an average of 8 treatments.

In the group with involutional psychoses 20 patients were treated. Of these, 18 (90 per cent) recovered; 1 (5 per cent) showed improvement, and 1, a woman aged 72, who had an agitated depression and had been at the hospital for ten years, showed no improvement.

In the group with manic-depressive psychosis, depressive type, 48 patients were treated. Of these, 30 (61 per cent) recovered; the condition of 9 (19 per cent) was much improved; that of 4 (9 per cent) showed improvement, and that of 5 (10 per cent) did not improve. Of the 5 patients who showed no improvement, the treatment of 1 was discontinued because of a complication affecting the respiratory tract; 1 died of a secondary infection, and 1 had a fracture as a result of electric shock. Incidentally, this was the only fracture we had during the year. (We use curare routinely.) One patient would recover from his depression only to relapse in a few days. The last patient of the group who showed no improvement only became confused.

In the group with manic-depressive psychoses, manic type, 17 patients were treated. Of these, 8 (47 per cent) recovered; 5 (30 per cent) showed much improvement; 1 (6 per cent) showed improvement, and 3 (17 per cent) showed no improvement. Most of the patients in this group had to have repeated courses of therapy.

In the group with schizophrenia 8 patients were treated. Of these, 1 (13 per cent) was much improved; 1 was improved, and 5 (60 per cent) did not improve.

In the group with psychoneuroses 8 patients were treated. Of these, none recovered; 1 (12 per cent) showed much improvement; 4 (50 per cent) showed improvement, and 3 (38 per cent) showed no improvement. The patient whose condition was much improved was homosexual, in a panic state. A follow-up study at the end of a month revealed that she was incapacitated by her psychoneurosis.

In the group with the undiagnosed psychoneuroses 15 patients were treated. Of these, 3 (20 per cent) recovered; 3 (20 per cent) showed much improvement; 7 (47 per cent) showed improvement, and 2 (13 per cent) showed no improvement. The 3 patients who recovered and 2 of the patients who manifested considerable improvement had agitated states.

These data support earlier statistics on electric shock (Smith, L. H.; Hastings, D. W., and Hughes, J.: *Am. J. Psychiat.* **100**:351 (Nov.) 1943). The rates of recovery are essentially the same except for the involutional group, for whom the rate rose from 70 to 90 per cent.

In general, agitation, depression, confusion and perplexity are the symptoms most favorably influenced by electric shock.

DISCUSSION

DR. N. W. WINKELMAN: Within the last few years my associates and I have been giving daily electric shock treatments to patients whose physical condition warrants such a heroic measure. Treatments are frequently given daily for eight to ten days, and the results have been much better than with the regimen of three treatments a week. The confusion is much greater than with the spaced treatments. At times a state is produced which resembles amentia. With patients in the manic stage of manic-depressive psychosis our results have not been good. Treatment apparently affects them only to a minor degree. It is our rule now to keep patients in the hospital two or three weeks after the cessation of shock therapy. The general statistics of the Philadelphia Psychiatric Hospital agree closely with those presented by Dr. Wright except those for the manic phase of the manic-depressive psychosis.

DR. HAROLD D. PALMER: Dr. Winkelman, do you use curare or any other means of modifying the severity of the convulsions?

DR. N. W. WINKELMAN: We do not use curare. We have had no fractures. We have the patient on a molded bed and keep the shoulders and hips down with firm pressure. Recently I have attempted to employ the dose which produces a slow, delayed reaction but does not cause the initial terrific jerking of the body.

The patient turns his head slowly, and then convulsive movements set in. If that dose can be gaged, one avoids much trouble.

DR. HAROLD D. PALMER: What voltage is used, and where are the electrodes applied?

DR. N. W. WINKELMAN: The reaction is a delayed general one. We begin with a low voltage and increase it gradually until the desired effect is obtained. The electrodes are placed on each side of the frontal poles.

DR. THOMAS WRIGHT JR.: We have found the shock which produces the petit mal reactions of no value; this was particularly true for a patient in whom we did not want to induce a generalized convulsion.

DR. JOSEPH HUGHES: How soon after admission should a patient be treated?

DR. THOMAS WRIGHT JR.: We think that electric shock should be used cautiously. One must not forget that patients recovered before the introduction of shock therapy. We study each patient thoroughly before we consider treatment. A great many patients are rushed into electric shock who would do well under hospital care alone in a month or two.

DR. MATTHEW T. MOORE: Many patients, particularly psychoneurotic and mildly depressed ones, respond favorably to conservative methods of psychotherapy, and much damage can be done if such persons are subjected to shock therapy. The psychic trauma, through the inference that the patient has a true psychosis, may bring about irreparable harm. There is still a difference of opinion with regard to whether morphologic change is produced in the brain. Although I have maintained that such damage does not occur, there must be some biochemical change within the ganglion cells themselves. Moreover, the indiscriminate application of electric shock to the brain over a long period may bring about changes resulting in rise in blood pressure. We have observed in a fairly large series of patients that the blood pressures have been very high.

DR. JAMES J. WAYGOOD: My colleagues and I are treating psychoneurotic patients with electric shock, I think with benefit. The depression and anxiety disappear, even though the patient may not completely recover. Of the group so treated, only 1 was said to be "much improved"; I think that in our practice a fair percentage of patients may be considered as considerably benefited.

Role of the Cortical Respiratory Center in the Production of Respiratory Distress During Electric Shock Therapy. DR. ROBERT G. HEATH.

In the reports on complications of electric shock, one is impressed by the large number of patients who have prolonged apnea, as well as the number of "unexplained" deaths from respiratory failure. The violent physical activity may explain cardiac failure, but the cause of deaths from respiratory failure remains unexplained, even after careful histopathologic studies. Prolonged apnea has been the only consistent complication at the Pennsylvania Hospital, and Brill and Kalinowsky reported (*Psychiatric Quart.* **16**:351 [April] 1942) that the only danger with electric shock therapy is postconvulsive arrest of respiration.

The theory of a cortical respiratory center was supported by many early investigators. Bucy and Case (*J. Nerv. & Ment. Dis.* **84**:156 [Aug.] 1936) did much to clarify this earlier work with carefully controlled experiments by stimulation of a field comparable to Brodmann's area 6b. During a craniotomy on a human patient they stimulated this area and produced complete cessation of respiration for fifteen seconds. Wilbur K. Smith (*J. Neurophysiol.* **1**:55 [Jan.] 1938) likewise produced cessation of respiration by stimulation of this area.

In relation to the exterior of the skull, this area is roughly situated midway between the orbit and the external auditory meatus and about 1.5 inches (3.8 cm.) above a line connecting these two points. Conventional electric shock therapy frequently reveals that it lies directly in the path of the greatest strength of the electric current.

At the Philadelphia General Hospital my associates and I have been altering the position of the electrodes and have found that when area 6b is approached, respirations frequently cease completely, with resultant pronounced cyanosis. Since there is no convulsion with this treatment, coincident muscular activity cannot be considered a factor.

Recently we have been able to continue treatment in cases in which it would otherwise have been terminated by moving the electrodes nearer the vertex, approximately over the area 6a, which has been observed to have a respiration-accelerating quality. Also, with this change in position we have had no prolonged apnea.

DISCUSSION

DR. THOMAS WRIGHT JR.: I should like to add something to Dr. Heath's statement. Only yesterday my associates and I, in treating a patient, used the large electrodes. She had a great deal of difficulty in breathing. We moved the electrodes, and she finally began to breathe well. Today we moved the electrodes farther toward the midline, and she had no difficulty in breathing.

DR. THEODORE L. DEHNE: Of about 170 patients whom my colleagues and I have treated with electric shock, 2 died suddenly of causes which were not satisfactorily explained. The first patient, a woman aged about 50, with involutional melancholia, was in good physical condition at the time electric shock therapy was begun. Eighteen hours after her fourth convulsion she died suddenly, of what was believed at the time to be disease of the coronary arteries. Permission for autopsy was refused. The second patient, a man aged 42, who was thought to be in satisfactory health, died suddenly twenty-four hours after his third convulsion. The terminal symptoms seemed to be those of respiratory failure. Autopsy revealed no adequate cause for the death.

DR. N. W. WINKELMAN: Some patients at the Philadelphia General Hospital who died of acute thrombosis of the coronary arteries have had no gross changes in the heart. This is because death was so sudden that the changes in the heart muscle did not become "fixed." The fact that a cause of death is not discovered does not eliminate acute coronary thrombosis.

DR. THEODORE L. DEHNE: How does one make a diagnosis of disease of the coronary arteries if there are no changes referable to these vessels?

DR. N. W. WINKELMAN: Often the pathologist reports "No cause for death apparent," but disease of the coronary arteries is suspected from the history. If there are no gross changes in the body or the brain, the best guess is disease of the coronary arteries, probably precipitated by electric shock.

Replacement of Convulsive Attacks by Psychoses. DR. EARL D. BOND.

A case is presented in which a patient expressed herself in temper tantrums for twenty years and then

had epileptic attacks daily for another twenty years and periods of classic manic-depressive excitement, interrupted by short depressions, for a third twenty years.

DISCUSSION

DR. ROBERT A. MATTHEWS: In a recent article on cessation of asthmatic attacks, it was pointed out that among some 10,000 patients in state hospitals for mental disease only 5 had asthma. This observation suggests a psychosomatic relationship.

DR. O. SPURGEON ENGLISH: Dr. Bond's paper reminds me of the case of a woman aged 27 who had attacks of falling asleep. The diagnosis of narcolepsy was considered, and her disorder was treated accordingly. A depression developed which lasted a year, at the end of which there was a mild hypomanic phase. Psychoanalytic treatment, carried on for about eighteen months, disclosed many factors in her personality which seemed to be related to her depression. One of the last difficulties to clear up were the attacks of falling asleep. Since I felt that her symptoms were psychogenic, I focused attention on the emotions connected with falling asleep, and before her treatment was completed her attacks subsided. According to her last report, she had not been troubled by the spells of falling asleep for about fourteen months. I regarded the attacks as representing a momentary departure from reality, a response to a need to escape from what was going on around her, and I worked with her on that basis. I think the spells of falling asleep were connected with the factors that caused the depression. The case seems to be somewhat similar to the one Dr. Bond has described.

DR. ELMER V. EYMAN: In connection with Dr. Matthews' comments, I wish to mention the case of a woman with manic-depressive psychosis who was subject to hay fever, but who never had hay fever during the psychotic attacks. One summer her husband called to say that his wife would soon be entering the hospital again, although her condition at the time was good. When asked for his reason for this opinion, he said that as the hay fever season was well under way and his wife was free from symptoms of the disorder, he was certain that a psychotic attack was impending. The woman did enter the hospital, with a manic attack, within a short time.

DR. LAUREN H. SMITH: Some years ago I had a patient with what appeared to be paranoid dementia precox. She had fixed delusions of infidelity on the part of her husband. Finally, after she had been ill for some years, the husband did run around with another woman. When the patient learned of this from her daughter, she recovered from the apparent mental illness in twenty-four hours.

DR. WILLIAM L. LONG: During the past ten years I have interested myself in the relation of somatic complaints and depression. I have worked for ten years in the allergy clinic, and twice a week I see as many as 50 patients with asthma, hay fever and eczema. During that time I have practically never encountered a patient with a depression. The patients are annoyed that they are sick, but they are not depressed. As a rule, they are free from psychoneuroses, and it may be that their asthma gives them the mental outlet that in other persons leads to depression and neurotic symptoms.

The Electroencephalogram as a Diagnostic Aid. DR. JOSEPH HUGHES.

Electroencephalography is indicated as a diagnostic procedure in all cases of persistent headache, fainting spells or convulsive seizures, as well as in cases of head trauma or any other condition which affects the cerebral cortex.

The normal electrical pulsations in the brain arise as the result of activity in the ganglion cells of the cortical gray matter. Normally these cells give rise to an electrical pulsation which appears in the electroencephalogram in a 9 to 11 per second rhythm with an amplitude of 10 to 30 microvolts. Abnormalities in the electroencephalogram consist of slowing in this pulsation and change in amplitude. Psychologic activity may suppress normal rhythm temporarily but does not give rise to any established change in amplitude or rate.

The electroencephalogram records electrical activity; it does not establish a clinical diagnosis. However, by interpretation of the electroencephalographic record in the light of the clinical history and the results of psychiatric and neurologic examinations, a great deal of useful diagnostic information can be obtained.

A single electroencephalogram will give positive evidence of epilepsy in about 80 per cent of cases. In this condition the frontal lobes show the greatest degree of electrical abnormality. Except for the spike-wave formations seen in some cases of petit mal, no electroencephalographic tracing is characteristic of this disease, nor can petit mal or grand mal be differentiated from each other on the basis of the electroencephalographic pattern.

Patients with behavior problems due to encephalitis or other organic causes may show abnormal tracings, the percentage depending on whether the cortex has been affected. A great deal has been written about the characteristic electroencephalographic patterns of children with behavior problems. It is an interesting corollary that a large percentage of delinquent children show no such abnormalities. In a recent survey by Hughes and Stewart of 250 boys placed in a corrective institution because of delinquency, less than 10 per cent were found to have definitely abnormal electroencephalographic tracings.

Tumors of the brain or cerebral metastasis from a carcinoma may be detected in about 90 to 95 per cent of cases in which the lesion has affected the cortex. Head trauma severe enough to produce a fracture or a concussion always results in electroencephalographic changes. These alterations may persist from three to six months after clinical symptoms have disappeared. Epilepsy is a frequent sequel of trauma. Its development may be expected in patients who fail to reestablish a normal pattern of electrical activity after an injury to the head. Dementia paralytica usually slows the cerebral pulsation and decreases its amplitude. Meningitis produces slow abnormal waves. Degenerative conditions, such as Pick's or Alzheimer's disease, also produce abnormalities. Cerebral arteriosclerosis affects the electroencephalogram to a degree which parallels the cortical involvement.

Clinical Observations on Patients with Behavior Disorders Who Show Abnormal Electroencephalograms. DR. ROBERT A. MATTHEWS.

The cases of 5 patients, with ages ranging from 6 to 20 years, who exhibited behavior disorders and abnormal electroencephalograms are reported. In addition to their calling attention to deviation of behavior as the odd expression of an underlying pathologic condition in the great integrating organ of the body, the central nervous system, these cases serve to pose several questions:

What can be done to prevent such sequelae of the virus diseases of childhood? Are these children con-

stitutionally of the chronic aggressive type, so ably discussed before this society several years ago by Dr. Gerald Pearson (The Chronically Aggressive Child, ARCH. NEUROL. & PSYCHIAT. **41**:641 [March] 1939)? If so, does the organic factor serve merely as a release of previously existing personality patterns, or is the behavior disorder the direct outgrowth of an acquired pathologic process in the central nervous system? What treatment can be instituted that may prove beneficial, and should it be psychologic or physiologic or both?

DISCUSSION

DR. HAROLD D. PALMER: In our study of behavior disorders, my associates and I have encountered 39 cases in which abnormal electroencephalograms were present. These tracings were interpreted by Dr. Hughes as indicating varying degrees of pathologic changes, ranging from simple cortical dysrhythmia to epilepsy. In many cases Dr. Hughes expressed the opinion that the tracings were similar to those obtained in cases of postencephalitic parkinsonism. The whole concept of the behavior disorder assumes a kind of related pattern, in which the qualities of the so-called postencephalitic and post-traumatic behavior disorders are predominant. Our observations lead us to the conclusion that there is a kind of dysrhythmic ideation, emotion and conduct. Some of the patients with these disorders had brain waves closely resembling those associated with epilepsy, although none had a history of attacks of grand mal, petit mal or psychomotor equivalent.

In many of these cases psychotherapy had been carried out for months or years, without benefit. The real test of the significance of these changes in brain waves is to be found in the response to treatment aimed at an alteration in the chemistry of the brain. Bradley, Jasper and others observed that amphetamine tended to correct the abnormal waves and improve the behavior in several cases. We have found this to be true. We have also employed the ketogenic diet, diphenylhydantoin sodium and small doses of phenobarbital, with good results.

It seems to me that in the kind of study which Dr. Matthews has made, and in our own work, one is crossing the borderline between the functional and the organic. One finds more and more instances in which neurotic-like states and behavior problems are related to underlying neurologic disease and consequently respond to treatment aimed at the correction of these organic and chemical disturbances, rather than to psychotherapy, which is aimed at the results of these disturbances.

ILLINOIS PSYCHIATRIC SOCIETY

FRANCIS J. GERTY, M.D., *President*

Regular Meeting, May 22, 1943

Hysteria and Malingering in Nurses. DR. I. R. SONENTHAL, Chicago.

A review of the literature on the emotional problems of nurses reveals a paucity of information. In the present paper definitions of malingering are cited (Hinsie, L. E., and Shatzky, J.: Psychiatric Dictionary, New York, Oxford University Press, 1940), and the psychology of malingering is discussed, with special reference to an article by Menninger (Psychology of a Certain Type of Malingering, ARCH. NEUROL. & PSYCHIAT. **33**:507 [March] 1935).

The case histories of 5 nurses who were patients in the medical ward are presented. The first deals with the production of hypoglycemic states which caused convulsions and led to operation for an adenoma of the pancreas; the second, with ingestion of large amounts of thyroid; the third, with the taking of phenobarbital; the fourth, with the production of symptoms diagnosed as indicative of a blood dyscrasia, and the fifth, with the apparent production of a prolonged, unexplained fever by the patient's tampering with the thermometer.

In the discussion two points are made: 1. The medical training of the patients aided them in the production of symptoms, and (2) the fact that they were medical personnel led to their not being suspected for a long time.

The relation between malingering and suicide is commented on.

In conclusion, reference is made to a reason for the physician's reaction to malingering; it is shown that in none of the cases were the goals for material gain, and the malingerer is classified with the neurotic or the psychopathic personality.

DISCUSSION

DR. FRANZ ALEXANDER, Chicago: I have little to add to this interesting paper. The case histories are convincing. It is valid to stress the presence of unconscious factors in most cases of malingering. The malingerer tries to evade some difficult situation, and there is no question that unconscious factors often play a decisive role.

On the other hand, there are known cases of malingering in which conscious motives are decisive. During World War I, among soldiers who were exhausted and wanted to get away from the front by any means, artificial infection with gonorrhea was occasionally practiced, the urethral secretion of a soldier who had a recurrence in the trenches and was sent back for treatment, being used. There may also be unconscious motives in such cases, but I think the conscious factor is predominant.

Dr. Sonenthal was hesitant about bringing up the relation of malingering to nursing. There is an interesting psychologic consideration. The nurse's psychologic situation is not an easy one. Her duty is to take care of other people all the time, whether she is equal to it or not. Whenever her dependent tendencies are aroused, they are greatly increased by her being continuously exposed to sick people who have the right to be taken care of. It is somewhat similar to the situation which is occasionally experienced in large families, in which the oldest daughter has to take responsibility for six or seven younger children. Under such circumstances one can often see her tremendous desire to be a small child, the envy of the smaller ones, and a repudiation of the imposed role of mother. Nurses are continuously exposed to a similar emotional strain. That they occasionally succumb to the temptation and wish to be sick themselves is intelligible. This wish to escape into sickness, together with the opportunity and a knowledge of symptoms, would seem to make them easier victims of malingering than many people who are not exposed constantly to this emotional difficulty. Therefore I should not be surprised if nurses did show a high percentage of malingering. However, there may be other occupations in which similar emotional conditions prevail.

DR. A. A. LOW, Chicago: Dr. Sonenthal has again emphasized the claim so frequently made that no clear distinction exists between malingering and hysteria. There are, however, the self-inflicted injuries in army service which Dr. Alexander mentioned as clearcut evidence of conscious and intentional self mutilation. That in many instances of such malingering hysteria plays no, or only a minor, part is generally agreed. Of more

significant interest is the question whether malingering is observed with respect to mental disease. It is known that Weir Mitchell took the view that mental disease may lend itself to simulation but that the simulant runs the risk of spending months or years in restraint, an event which would cancel any gain he might expect from his simulation. The simple view that war service is preferable to existence in an asylum may have been justifiable in Civil War days but is hardly applicable at present. Nevertheless, in World War I it was the consensus that mental disease cannot be, and is not, simulated. Then Dr. O. Klieneberger (*Ztschr. f. d. ges. Neurol. u. Psychiat* **71**:239, 1921) reported his experiences with German officers in a British prison camp. He trained the officers to simulate discrete psychiatric and neurologic syndromes, with the result that several of them were exchanged as invalids. Since then the controversy concerning the possibility of simulation of mental disease seems to have died down. However, it may safely be claimed that simulation of mental disease must be difficult and requires patient coaching on the part of the expert.

DR. C. F. READ, Elgin, Ill.: I have seen many cases of traumatic neuroses. For example, a laborer, perhaps 50 years old and approaching the close of his active physical life, has a bump on his head. Perhaps he feels fairly well for a few days, makes no complaint and then begins to have symptoms, usually dizziness and headache and perhaps some difficulty with vision and sleep. Such persons, as I have seen them, have all been a rather simple folk. They may have an opportunity to obtain compensation that will set them up in some little business. Perhaps they are afraid of not being able to work again as they used to, and they desire the sympathy of the family. Are these persons malingerers? How much is on a conscious level? In examination for testimony before an industrial commission one finds no objective symptoms, nor is anything noted in the neurologic examination that will substantiate the claims of the plaintiff. I wonder how far this goes beyond the desire for compensation, and whether the symptoms are not merely the continuation of those experienced immediately after the injury, for the purpose of gain. How conscious is this attempt, and what is its basis, other than the instinct for self preservation?

DR. L. H. ZIEGLER, Wauwatosa, Wis.: In the course of a similar clinical experience during the last twenty years, although in general not associated with nurses, I have occasionally seen a patient, not unlike the patients described, who struggled to conceal or camouflage the symptoms of an insidiously oncoming affective or schizophrenic disorder, which could not be diagnosed until later. Some of these patients tried to influence the physician to make a diagnosis of a physical disorder, rather than of nervousness or mental disease, which they feared. Of course, nurses would know better than others how to do this. In the light of such developments, I have felt that the word malingering should be used with caution.

DR. I. R. SONENTHAL, Chicago: In answer to Dr. Read, the choice of malingering as a reaction may easily be the subject of much discussion. When a person chooses malingering as a mode of reaction, there are definite factors in that personality (with others in the same setting) which produce that type of reaction. The choice of malingering is analogous to that of any neurosis or psychosis as a solution to a difficult situation. With respect to the selection of cases in my report, they represented a period of six years, and the nurses were not from this hospital, but were referred from various hospitals in the city because the diagnosis of their condition was unusually difficult. I agree in principle that physicians and medical students could be included in such a study, although in the period reviewed there were no similar cases among physicians, to my knowledge.

Fundamental Concepts of Psychosomatic Research: Psychogenesis; Conversion; Specificity.
DR. FRANZ ALEXANDER, Chicago.

Psychogenesis.—The term "psychogenic" refers to physiologic processes consisting of excitations in the nervous system which are perceived subjectively in the form of emotions, ideas or wishes and which can be studied by psychologic methods. Psychosomatic research deals with such processes, in which certain links in the causal chain of events lend themselves more readily, in the present state of knowledge, to a study by psychologic than by physiologic methods.

Conversion.—Essentially, a hysterical conversion symptom is nothing but an unusual innervation; it does not differ in principle from any other voluntary innervation or from such expressive movements as speech, laughter or weeping. The meaning of a conversion symptom was originally definite; it was a symbolic substitute for an unbearable emotion. It was assumed that the symptom relieved, at least to some degree, the tension produced by the repression of the unbearable emotion. It was considered a kind of physical abreaction, or equivalent, of an unconscious emotional tension.

It is not valid to extend the original concept of hysterical conversion to all forms of psychogenic disturbances of the body, particularly to those of the visceral vegetative organs. For example, in emotionally conditioned hypertension the elevation of the blood pressure is not the substitute expression of a repressed emotion, such as rage, but the normal physical accompaniment of the emotion. The elevated blood pressure does not relieve the anger in the least. It does not appear in place of an emotional tension. It simply accompanies the emotion of rage. It is an inseparable part of the total phenomena called rage. The same thing obtains for other vegetative disturbances. The pathologic nature of such vegetative disturbances consists in their chronicity. There are chronic, unrelieved emotional tensions which cause chronic vegetative disturbances. The quality of the physiologic response is normal; only its chronic nature is morbid.

Therefore it seems advisable to differentiate between hysterical conversion and vegetative neurosis. Their similarities are superficial; both conditions are psychogenic. The mechanisms involved, however, are fundamentally different, both psychodynamically and physiologically. A hysterical conversion symptom is an attempt to relieve an emotional tension in a symbolic way; it is a symbolic expression of a definite emotional content. This mechanism is restricted to the voluntary neuromuscular or sensory perceptive systems, the function of which is to express and relieve emotions. A vegetative neurosis consists of a psychogenic dysfunction of a vegetative organ which is not under control of the voluntary neuromuscular system. The vegetative symptom is not a substitute expression of the emotion but its normal physiologic component. It is assumed that for every emotional state there is a corresponding distribution of vegetative innervation. When the organism is ready to fight, the vegetative organs are relatively relaxed, whereas the muscular system and the lungs are in a state of preparation for activity. The emotional attitude accompanying and preceding intake of food is, again, accompanied by a different distribution of vegetative tonus. One type of vegetative disturbance occurs as a result of an emotional retreat

from strain. If, for example, the patient with a neurosis referable to the stomach breaks down under an excessive load of responsibility, he recoils from his habitual overactivity and assumes the vegetative mood of the state that accompanies digestion, to which his alimentary tract reacts with continuous hyperactivity. According to all indications, an outwardly directed, active aggressive state is associated with a sustained excess of tonus of the sympathetic-adrenal system, from which the person when exhausted may retreat into the opposite attitude, in which the tonus of the vagoinsular system is increased. This recoil from exaggerated outward activity and strain may be called "vegetative retreat." It is characterized by increased tonus of the parasympathetic system, possibly associated with simultaneous relaxation of sympathetic-adrenal tonus. This may assume different forms, consisting in some hyperactivity of visceral organs as a result of parasympathetic excitation, such as hypersecretion and hypermotility of the stomach, diarrhea or psychogenic hyperinsulinism (psychogenic hypoglycemia).

Specificity.—According to one school of thought, there is no specficity of correlation. Any emotional tension may influence any vegetative system. The choice of the symptoms may depend on the history of the patient and on his constitution. The other heuristic assumption, which has guided the work of the Chicago Psychoanalytic Institute, is that the physiologic response differs with the emotional tension and that, consequently, vegetative dysfunctions result from specific emotional constellations. It was found, for example, that symptoms of gastric neurosis have a different psychologic setup from those of emotional diarrhea or constipation; patients with cardiac disorders differ in their emotional background from asthmatic patients. Hypertensive patients, again, have a different psychodynamic constellation. To what extent constitutional factors influence the picture and to what extent a preexisting organic pathologic condition or sensitivity is responsible are questions to be decided by further clinical studies.

DISCUSSION

DR. WARREN S. MCCULLOCH, Chicago: Most, and first, consideration should be given to Dr. Alexander's opening statement concerning the elimination, once and for all, from the publications of psychosomatic medicine of any discussion of problems of the relation of mind and body. I feel like giving three cheers for the indifferent monism that underlies such a comment. There is a dichotomy in medicine which has grown increasingly. It is a consequence of the division into specialties. The psychiatric, particularly the psychoanalytic, approach has produced one group; the organic approach to the physiology of particular organs and disease processes has made organicists of another group. It has become difficult for these two groups to talk to each other. I am afraid that there is still in the minds of most persons here, and will be for years, that difficulty which concerned, and still concerns, many thinking people—the dichotomy of mind and body. There is still the attempt to explain "the leap from psyche to soma."

Dr. Alexander uses two types of terminology: the one when he speaks of mental affairs and the other when he speaks of physical affairs. It is appropriate that he should speak in mental terms of psychologic processes, for these exhibit ideas and intentions. It is equally appropriate that he should speak in physical terms of bodily processes, for these exhibit matter and energy; the difficulty, however, is that no one has ever managed to conceive how the patient—the monad—can have such a divorcement of the psychologic and the physiologic aspect of his nature. I may be thought to be exaggerating the difficulty, but there have appeared within the last few years two books which tilt at the same windmill. In one, entitled "Man on His Nature" (London, Cambridge University Press, 1938), Sherrington, the marvelously honest physiologist, attempts to make head and tail of the relation of mind and body, but is frustrated because in that world "mind goes more ghostly than a ghost." In the other, entitled "The Place of Value in a World of Fact," by Wolfgang Köhler (the founder of gestalt psychology), one is convinced that the author, in spite of his endless searching, has not found the place of value in the world of fact. Such was the unsatisfactory state of the theory until recently.

However, there recently has appeared an article by Rosenblueth and collaborators (*Philos. Sc.* **10**:18, 1943) which gives a general presentation of systems responding to the outside world, that is, to the strains or impulses impingent on such systems from the outside world. Systems are classified according to the way in which they respond. In particular, the authors discuss the type of behavior characteristic of systems in which the system so responds as to decrease the difference between the impinging disturbance and the energy already present in the system. Certain of these systems depend on disturbances traveling in closed paths, or circuits, and respond in such a way as to decrease the difference between the adventitious disturbance and the disturbance traveling in the closed system. Two such familiar devices are the self-tuning radio, which seeks its station, and the self-directing torpedo, which hunts its prey. Engineers call such devices servile; psychologists call them appetitive. Psychologists refer to such behavior as motivated, goal directed or purposeful, and organisms are known to contain systems of the type in question. In other words, organisms and all such devices have those aspects of behavior which are utilized in the definition of purposiveness. One can then define in purely mechanistic terms (or have a purely mechanistic conception of) the attempt to reach any goal.

At present the other mental aspect of behavior—its ideational or rational, formal or logical aspect—is coming to the fore. Work on this phase was begun some years ago in the department of mathematical biophysics of the University of Chicago and should be coming to fruition in the next year or two. Under these circumstances, I am not surprised that the *Journal of Psychosomatic Medicine* should receive articles on the problem of the relation of mind and body. One does resent the existing hiatus between the mental and the physical terminology. The problem is today being attacked in a realistic fashion. So while one does at the moment think of the "leap from psyche to soma," one is busy bridging the gap between mental and physical processes. To this audience it is interesting that such a bridge is being formed through the demonstration that the systems which are like the nervous system necessarily show those aspects of behavior that are called "mental"—namely, ideas and purposes. So much for the first part of Dr. Alexander's paper.

The second question which he has raised and answered concerns the distinction between those structures which are under voluntary control, and hence can be used relatively easily in symbolic fashion because they deal with the outside world, and those structures which are not under voluntary control or of use in handling the outside world, but readjust the immediate environment of the nervous system to its demands—the autonomic nervous system and the glands under its control. This point needs little discussion, for it is clear that Dr.

Alexander has put his finger on one of the crucial differences between the two systems, both in their function and in their abuse, or disease. The first system is as flexible as man's adjustments to the external world, and the second, as stereotyped as man's primordial emotions.

Here another consideration prompts me to ask a further question. Neurophysiologists originally thought in terms of mere conduction. Later they came to think in terms of reflexes. Today there is a growing tendency to think in terms of closed circuits. In the case of the so-called voluntary nervous system, the circuit closes through the world outside the organism and forms the link between one's actions and one's resultant sensations. In the case of the autonomic nervous system, the circuit closes within the body by means of glands and smooth muscle, the action of which, in turn, affects the nervous system. But there is a third possibility; I wonder whether Dr. Alexander has yet considered it. There is within the nervous system itself an enormous number of closed circuits. My question is whether these closed circuits may not themselves prove an even more fruitful field for psychiatric study than any one has hitherto dreamed.

Dr. Alexander's last question concerned the relation of the autonomic nervous system to the emotions. He asked to what extent a specific emotion gives rise to a specific autonomic outflow and suggested that the relation was relatively constant. In this I heartily agree with him. Inevitable specificities of nervous energies are involved in the emotions. Even particular pathways in the nervous system are involved in particular emotions. These pathways are related definitely to particular organs and to particular glands and smooth muscles. Thus one must expect particular organs to be involved in particular emotions. The other side of the question obviously depends on the organs of the particular pathways, particularly if they are defective. Inherited bent and learning may determine what particular emotion the patient experiences under given conditions, but when all is said and done, I heartily agree with Dr. Alexander that a particular emotion is related to an autonomic discharge to particular organs, though neither the emotion nor the discharge is completely determined by that relation.

Dr. Meyer Solomon, Chicago: First, I wish to compliment Dr. Alexander on his critical and common sense approach to this whole problem. Many psychiatrists, like himself, have been battling with the problem of mind and body, struggling to get a satisfactory clinical approach. I wonder whether the term "psychophysiologic medicine" or "organismic medicine" is not preferable to "psychosomatic medicine."

One of the problems is the use of the terms mind and psyche without definition.

The following clinical approach seems useful and practical: For practical purposes bodily activities can be divided into three types: psychologic; skeletal (voluntary, ambulatory, sensorimotor, postural and projicient), and visceral (involuntary and vegetative). Ordinarily, these levels of activity are interrelated, interdependent and integrated into a unit. The psychologic level may be referred to as psychologic or mental and includes such special bodily activities of an internal, subjective nature as thinking, feeling, wishing, reasoning and imagining. It has been customary to use the generic term "the mind" or "the psyche" to refer to this special group of bodily activities, and then the mistake is made of speaking of "the mind" as if it were a separate entity which is causative and does things. In fact, there is no such entity as "the mind"; there are mental, or psychologic, activities. Psychosomatic, or psychophysiologic, or organismic medicine, which deals with what is commonly referred to as the influence of "the mind" on the body, is concerned with the interrelation of the three levels already mentioned, namely, the psychologic, the skeletal and the visceral. Dr. Alexander has discussed critically the question of the relation of the psychologic to the skeletal and the visceral level. This brings up the question of immediate versus remote and direct versus indirect effects. An immediate effect is emotional behavior, with psychologic, skeletal and visceral upheaval; a remote effect is loss of weight following poor sleep and poor appetite of psychologic origin; a direct effect is voluntary movement of the skeletal system (head, trunk, extremities), and an indirect effect is vegetative activity for the maintenance and support of voluntary activities. This brings up such problems as that of so-called voluntary acceleration of the heart rate and the relation to sensory function.

In his presentation, therefore, Dr. Alexander has expressed a sensible, basic point of view with respect to fundamental problems in this complicated field of medicine.

Dr. Franz Alexander, Chicago: I wish to thank all the discussants for their instructive comments. I shall clarify one point only. Let it be assumed that two chess players are sitting opposite each other, and that I am watching their playing. I can understand their moves through certain logical deductions; that is, I can describe their motivations in psychologic terms. Chess playing is a rather complicated procedure, but the motives of the players in making the moves can be reconstructed with complete precision. Now let it be assumed, for example, that fifty years hence one will be able to describe with equal precision all the neurophysiologic processes which took place in the brain of the players while they are making their different moves. Then, on one side, we shall be able to describe the mental processes taking place in the minds of the players in psychologic terms and, on the other, the same processes in neurophysiologic, and ultimately in physicochemical terms. Both descriptions will represent complete causality: the one psychologic and the other physiologic.

Psychosomatic medicine deals with processes which, in the present state of knowledge, can best be approached partially by physiologic and partially by psychologic description.

One cannot use at present a homogeneous language in dealing with certain conditions. For example, in the case of psychogenic hypoglycemia one must describe the causal factors in psychologic terms, namely, those depressive ideas which are responsible for the vegetative innervations which lead to hypoglycemia. Perhaps at some future time these emotional factors may be described in physiologic terms and a homogeneous language used. How can that be done today with such complex psychologic phenomena as are involved when a patient becomes depressed because his sweetheart has left him? How can one describe in physicochemical terms the injury to his pride, his loss of interest in everything, his resentment? At present the only possible procedure is to deal with the emotional factors in psychologic terms and its physiologic effects in physiologic terms. In the future, with progressing knowledge of the physiology of the brain, a homogeneous physiologic description is conceivable, but even then it appears questionable whether one can dispense with detailed psychologic descriptions in an understanding of the patient's complex human relationships.

Book Reviews

The Boy Sex Offender and His Later Career. By Lewis J. Doshay, M.D., Ph.D. Price, $3.50. Pp. 217. New York: Grune & Stratton, Inc., 1943.

Dr. Doshay, psychiatrist to the Children's Courts in New York city, has written an important and needed book describing his findings in 256 cases of male juvenile sex offenders studied and treated at the clinics of the courts between June 1928 and June 1934. Sexual offenses accounted for less than 5 per cent of the acts for which delinquent boys were brought to court. At the time of the clinic study the ages of the boys ranged from 7 to 16 years, and at the time of writing they varied from 16 to 28 years. Seventy-five per cent of both groups were in the age range from 12 to 15 years, and the average age for the whole group was 13.6 years. The follow-up study was made from six to twelve years after the original court appearance. Female sex delinquents were not included in this study, and all mentally defective sex offenders were excluded. The boys were divided into two groups, one being the so-called primary group of 108, who were in court solely because of sex delinquencies, and the second the mixed group, of 148, whose delinquencies included sexual and other antisocial acts.

The author compares the two groups from the standpoint of family and home factors, factors concerned with the personalities of the parents, community factors and inherent traits in the boys, including temperament and behavior. His investigations reveal that children in the primary group came from homes of higher income, better housing and higher educational status.

With respect to the personalities of the parents, special emphasis was placed on such items as alcoholism, drug addiction, court records and desertion. It was found that the outstanding defects among the fathers in the primary group were alcoholism and desertion, which occurred in 37 per cent, whereas in 63 per cent of the fathers of the mixed group alcoholism, desertion, criminality, immorality and cruelty were noted. Poor community factors—for example, a bad neighborhood; unhealthy forms of recreation, such as poolrooms; maladjustment at school; occasional or no church attendance, and hazardous vocational interests, such as selling papers at night, shoe shining or entertaining in grills or saloons—were found for only 24.3 per cent of the primary group, as compared with 75.7 per cent of the mixed group.

In a study of the temperament and behavior of the boys, it was found that disorders such as surliness, callousness, cruelty, restlessness, stubbornness and aggressiveness appeared six to ten times as often in the mixed group as in the primary group. Of the types of sex offenses, the only item of notable difference was the occurrence of 12 instances of incest with sisters in the mixed group and of only 1 instance of attempted incest in the primary group. Otherwise, the types of sex offenses were the same and included all acts, such as fellatio, sodomy, exhibitionism, peeping and heterosexual experiences. Serious physical defects (tuberculosis, heart ailments, deafness and severe malnutrition) were present in 11.1 per cent of the primary group and in 3.4 per cent of the mixed group. Glandular defects were found in only 4.3 per cent of cases. The author emphasizes that delinquency, sexual or general, is not due to glandular disorders.

In the follow-up study, there were only 10 known instances of sex violations among 8 adult members of the mixed group and no instance of sex violations in the primary group. However, 2.8 per cent of the primary group and 25 per cent of the mixed group were involved in delinquencies in their adult life, including burglaries, assault, arson and forgery.

Dr. Doshay concludes that male juvenile sex delinquency is self curative, provided "the latent forces of shame and guilt, inherent in the moral-cultural pattern, are properly stimulated into action." He further points out that the outlook for juvenile delinquency in general is much better than that indicated by the works of the Gluecks, Healy and Bronner. Dr. Doshay's findings are in close accord with the results of follow-up studies in the Bellevue Hospital adolescent ward. Dr. Doshay further indicates the close cooperation between the judges of the Children's Courts and the physicians in following out recommendations for treatment, an observation which has also been made in the Bellevue studies.

It is my impression that the book in general is a real contribution to knowledge, not only of sexual delinquency but of juvenile delinquency in general, and that it is a book of definite value to probation officers, social workers, teachers and psychiatrists. It indicates that the prognosis, even for the most severe forms of juvenile delinquency, is much better than that indicated by many investigators. This book should serve as an added impetus to all workers in the field of child guidance and should spur one on to increase medical and social facilities for the treatment of these unfortunate youngsters.

Manual of Industrial Hygiene and Medical Service in War Industries. Prepared by the Division of Industrial Hygiene, National Institute of Health, United States Public Health Service. William M. Gafafer, D.Sc., editor. Price, $3.00. Pp. 508. Philadelphia: W. B. Saunders Company, 1943.

The rapid growth of industry necessitates a related increase in industrial health practice. The need for this volume was clearly foreseen by the Committee on Industrial Medicine of the Division of Medical Sciences of the National Research Council, and the preparation of the book was entrusted to the United States Public Health Service. Special chapters were written by an outstanding group of experts.

The volume is divided into three parts. Part 1 is concerned with the organization and operation of facilities. This portion of the book is headed by an excellent chapter on the war's influence on industrial hygiene, written by J. J. Bloomfield. Other chapters cover the problems of plant medical facilities; organization of a plant medical department; medical, nursing and dental services, and the organization of plant emergency medical service and its integration with that of the community.

Part 2 is concerned with the prevention and control of disease in industry. Here special chapters are devoted to the problem of occupational disease, occupational derivates, engineering control of air contamination, medical disease control, venereal disease control, health education, industrial psychiatry, industrial fatigue and nutrition in industry. This section is well done. Another portion of the volume is concerned with plant and community sanitation, heating, ventilation and illumination problems.

The third portion of the volume is concerned with the manpower problem, and careful consideration is given to problems of the maximal use of manpower, women in industry and absenteeism.

This book is highly recommended as a timely volume on industrial medicine. It is the best of its kind, is exceedingly well written and should be of great interest to every physician.

Convulsive Seizures: How to Deal with Them, a Manual for Patients, Their Families and Friends. By Tracy J. Putnam, M.D. Price $2. Pp. xv plus 168. Philadelphia: J. B. Lippincott Company, 1943.

This is a small book, but full of meat, and expressed in unusually readable terms. It is well within the capacity of the layman to understand; yet it includes the best of current thought on this important subject. The author is particularly to be commended for sounding a hopeful note without at the same time indulging in any Pollyanna attitude. He shows that while great advances in the knowledge of the disease have come about through the researches of the past few years, the investigations to come are even more important. He calls vigorously for greater public interest in the plight of persons unfortunate enough to have seizures, and at the same time urges the sufferers to help themselves. "Much remains to be done," he asserts, and proves this by pointing out in almost every chapter where the advances of the future may be anticipated.

The plan of the book is excellent. It is written not as a medical text, but strictly from the standpoint of the individual patient and for his benefit. Yet it takes up in succession causes, diagnosis, treatment and prognosis of convulsions, references to the literature and special problems of interest to lawyers and legislators. Brief summaries, almost aphorismic, are enclosed in boxes in connection with each chapter, so that he who runs may read. Sane and sensible directions for the management of the individual attack; serious, yet hopeful, suggestions for the planning of a career for the afflicted person; references to more elaborate treatises, with cautions against too much indigestible reading and any self medication—these are features that make this small volume one that can be placed in the hands of the patient with all reasonable assurance that it will be helpful.

News and Comment

THE AMERICAN BOARD OF NEUROLOGICAL SURGERY

Dr. Wilder Penfield, of Montreal, Canada, has been granted a certificate without examination by the American Board of Neurological Surgery.